# This Page Is Inserted by IFW Operations and is not a part of the Official Record

### **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

### IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

# (19) World Intellectual Property Organization International Bureau



### 

### (43) International Publication Date 27 June 2002 (27.06.2002)

### PCT

# (10) International Publication Number WO 02/50289 A1

(51) International Patent Classification<sup>7</sup>: C12N 15/79

(21) International Application Number: PCT/US01/50240

(22) International Filing Date:

19 December 2001 (19.12.2001)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

09/742,900 19 December 2000 (19.12.2000) US 60/302,885 5 July 2001 (05.07.2001) US 10/006,038 4 December 2001 (04.12.2001) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US 09/742,900 (CIP)
Filed on 19 December 2000 (19.12.2000)
US 60/302,885 (CIP)
Filed on 5 July 2001 (05.07.2001)
US 10/006,038 (CIP)
Filed on 4 December 2001 (04.12.2001)

(71) Applicants (for all designated States except US): SEM-BIOSYS GENETICS, INC. [CA/CA]; 110, 2985 - 23rd Avenue, N.E., Calgary, Alberta T1Y 7L3 (CA). SYN-GENTA PARTICIPATIONS AG [CH/CH]; Schwarzwaldallee 215, CH-4058 Basel (CH).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): VAN ROOIJEN, Gijs [NI./CA]; 3223 Bearspaw Drive N.W., Calgary, Alberta T2L 1T1 (CA). DECKERS, Harm [NI./CA]; 519, 18th Avenue N.W., Calgary, Alberta T2M 0T7 (CA). HEIFETZ, Peter, Bernard [US/US]; 10805 Birch Bluff Avenue, San Diego, CA 92131 (US). BRIGGS, Steven, P. [US/US]; 2454 Mango Way, DelMar, CA 92014 (US). DALMIA, Bipin, Kumar [IN/US]; 7353 Mannix Court, San Diego, CA 92122 (US). DEL VAL, Gregg [CH/US]; 5727 Erlanger Street, San Diego, CA 92122 (US). ZAPLACHINSKI, Steve [CA/US]; 5840 Dalmead Cres., Calgary, Alberta T3A 1E6 (CA). MOLONEY, Maurice [IE/US]; 34 Edgebrook Cove N.W., Calgary, Alberta T3A 5N5 (CA).
- (74) Agents: RAMOS, Robert, T. et al.; Campbell & Flores, LLP, 4350 La Jolla Village Drive, 6th Floor, San Diego, CA 92122-1246 (US).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

### Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY,

[Continued on next page]

(54) Title: METHODS FOR THE PRODUCTION OF MULTIMERIC PROTEINS, AND RELATED COMPOSITIONS

(57) Abstract: Improved methods for the production of multimeric-protein-complexes, such as redox proteins and immunoglobins, in association with oil bodies are described. The redox protein is enzymatically active when prepared in association with the oil bodies. Also provided are related nucleic acids, proteins, cells, plants, and compositions.



2/50289 A1

- BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- --- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,

- TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

#### Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

### METHODS FOR THE PRODUCTION OF MULTIMERIC PROTEINS, AND RELATED COMPOSITIONS

### **RELATED APPLICATIONS**

5

10

25

30

Benefit of priority under 35 U.S.C. §119(e) is claimed to U.S. provisional application Serial No. 60/302,885, filed July 5, 2001, to van Rooijen, et al., entitled "METHODS FOR THE PRODUCTION OF REDOX PROTEINS". This application is also a continuation-in-part of U.S. utility application Serial No. 10/006,038, filed December 4, 2001 to van Rooijen, et al., entitled "METHODS FOR THE PRODUCTION OF REDOX PROTEINS"; which is a continuation-in-part of U.S. utility application Serial No. 09/742,900, filed December 19, 2000 to Heifetz, et al., entitled "METHOD OF PRODUCTION AND DELIVERY OF THIOREDOXIN". This application is also a continuation-in-part of U.S. utility application Serial No. 09/742,900. The subject matter of each of the provisional and utility applications is incorporated herein by reference in its entirety.

#### 15 Field Of The Invention

The present invention relates to multimeric-protein-complexes, redox proteins, and recombinant polypeptides; and improved methods for their production.

### **BACKGROUND**

Multimeric proteins (i.e. proteins comprising multiple polypeptide chains) are a biologically and commercially important class of proteins. Antibodies for example are multimeric proteins which are used to treat a wide range of disease conditions. However in view of their complexity, multimeric proteins frequently represent significant manufacturing challenges.

Redox proteins are also a commercially important class of proteins with applications in a variety of different industries including the pharmaceutical, personal care and food industry. For example, the redox protein thioredoxin may be used in the manufacture of personal care products (Japanese Patent Applications JP9012471A2, JP103743A2, JP1129785A2), pharmaceutical compositions/products (Aota et al. (1996) J. Cardiov. Pharmacol. (1996) 27: 727-732) as well as to reduce protein allergens present in food products such as

-2-

milk (del Val et al. (1999) J. Allerg. Vlin. Immunol. 103: 690-697) and wheat (Buchanan et al. (1997) Proc. Natl. Acad. Sci. USA 94: 5372-5377).

However, there is a need in the art to further improve the methods for the recombinant expression of multimeric proteins, including redox proteins. The present invention satisfies this need and provides related advantages as well.

SUMMARY OF THE INVENTION

The present invention relates to novel and improved methods of producing a first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulin-polypeptide-chains, immunoglobulins, redox-fusion-polypeptides, and/or thioredoxin-related proteins; in association with oil bodies. Accordingly, provided herein are methods of producing a recombinant multimeric-protein-complex, said method comprising:

(a) producing in a cell comprising oil bodies, a first recombinant polypeptide and a second recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said multimeric-protein-complex; and (b) associating said multimeric-protein-complex with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said first recombinant polypeptide.

10

15

20

25

30

The method further contemplates isolating the oil bodies associated with said recombinant multimeric-protein-complex. The second recombinant polypeptide can be associated with a second oil-body-targeting-protein capable of associating with an oil body and said second recombinant polypeptide. Each of said oil-body-targeting-proteins can be an oil-body-protein or an immunoglobulin. The oil-body-targeting-protein can be an oleosin or caleosin. When the oil-body-targeting-protein can be an oleosin or caleosin, the first recombinant polypeptide can be fused to said oleosin or caleosin. Likewise, the second recombinant polypeptide can be fused to a second oleosin or second caleosin capable of associating with an oil body. The first and second recombinant polypeptides can be produced as a multimereic-fusion-protein comprising said first and second polypeptide, and can form a multimeric-protein-complex. The multimeric-protein-complex can be a heteromultimeric-protein-

complex, and the heteromultimeric-protein-complex can be an enzymatically active redox complex or an immunoglobulin. In one embodiment, the first recombinant polypeptide is capable of associating with said second recombinant polypeptide in the cell. In another embodiment, the first recombinant polypeptide can be a thioredoxin and the second recombinant polypeptide can be a thioredoxin-reductase. In particular embodiments, the thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be 10 an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In 15 this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. The cell can be a plant cell, such as a safflower cell, and the like.

Also provided herein is a method of expressing a recombinant multimericprotein-complex comprising a first and second recombinant polypeptide in a cell, said method comprising:

- 20 (a) introducing into a cell a first chimeric nucleic acid sequence comprising:
  - (i) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
  - (ii) a second nucleic acid sequence encoding a first recombinant polypeptide;
- 25 (b) introducing into said cell a second chimeric nucleic acid sequence comprising:
  - (i) a third nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
  - (ii) a fourth nucleic acid sequence encoding a second recombinant polypeptide;
- 30 (c) growing said cell under conditions to permit expression of said first and second recombinant polypeptide in a progeny cell comprising oil bodies wherein

-4-

said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimeric-protein-complex; and (d) associating said first recombinant polypeptide with an oil body through an oilbody-targeting-protein capable of associating with said oil bodies and said first recombinant polypeptide. This method further contemplates isolating from the progeny cell, oil bodies comprising the multimeric-protein-complex. The second recombinant polypeptide can be associated with a second oil-body-targetingprotein capable of associating with an oil body and second recombinant polypeptide. Each of said oil-body-targeting-proteins can be an oil-body-protein 10 or an immunoglobulin. The oil-body-targeting-protein can be an oleosin or caleosin. When the oil-body-targeting-protein is an oleosin or caleosin, the first recombinant polypeptide can be fused to said oleosin or caleosin. Likewise, the second recombinant polypeptide can be fused to a second oleosin or second caleosin capable of associating with an oil body. The first and second recombinant polypeptides can be produced as a multimereic-fusion-protein 15 comprising said first and second polypeptide, and can form a multimeric-proteincomplex. The multimeric-protein-complex can be a heteromultimeric-proteincomplex, and the heteromultimeric-protein-complex can be an enzymatically active redox complex or an immunoglobulin. In one embodiment, the first 20 recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimeric-protein-complex in said progeny cell. In another embodiment, the first recombinant polypeptide can be a thioredoxin and the second recombinant polypeptide can be a thioredoxin-reductase. In particular embodiments, the thioredoxin can be selected from the group consisting of SEQ 25 ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant 30 polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise

protein A, protein L or protein G. The cell can be a plant cell, such as a safflower cell, and the like.

Also provided herein are methods of producing in a plant a recombinant multimeric-protein-complex, said method comprising:

- (a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said oil bodies through an oil-body-targeting-protein;
  (b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide; and
- (c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex.
- The second recombinant polypeptide can be associated with oil bodies through a second oil-body-targeting-protein in the second plant. The oil bodies can be isolated from the progeny plant comprising said multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin, wherein the oil-body-protein can be an oleosin or caleosin. The first recombinant polypeptide can be fused to the oleosin or caleosin; and the second recombinant polypeptide can be fused to a second oleosin or second caleosin capable of associating with an oil body. The first and second recombinant polypeptide can form a multimeric-protein-complex, such as a
- can be an enzymatically active redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group

heteromultimeric-protein-complex, wherein the heteromultimeric-protein-complex

30 consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant

-6-

polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. The plant can be a safflower plant.

Also provided herein are chimeric nucleic acids encoding a multimericfusion-protein as described herein, said nucleic acid comprising:

(a) a first nucleic acid sequence encoding an oil-body-targeting-protein operatively linked in reading frame to;

(b) a second nucleic acid sequence encoding a first recombinant polypeptide; linked in reading frame to;

5

15

20

25

30

(c) a third nucleic acid sequence encoding a second recombinant polypeptide, wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin. The oil-body-protein can be an oleosin or caleosin. The multimeric-protein-complex can be a heteromultimeric-proteincomplex, and the first and second recombinant polypeptide can form an enzymatically active heteromultimeric redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. In yet another embodiment, positioned between the nucleic acid

sequence encoding an oil-body-targeting-protein and the nucleic acid sequence encoding a first recombinant polypeptide can be a linker nucleic acid sequence

-7-

encoding an oil-body-surface-avoiding linker amino acid sequence. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. Optionally, the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence that is also a non-proteolytic linker and said sequence encoding the first recombinant polypeptide.

10

15

20

25

Also provided herein are recombinant multimeric-fusion-proteins comprising (i) an oil-body-targeting-protein, or fragment thereof, (ii) a first recombinant polypeptide and a (iii) second recombinant polypeptide, wherein said first and second recombinant polypeptides are capable of forming a multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin, and the oil-body-protein can be an oleosin or a caleosin. The multimeric-fusion-protein can be a heteromultimericfusion-protein, wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. In yet another embodiment, positioned between the nucleic acid sequence encoding an oil-body-targeting-protein and the nucleic acid sequence encoding a first recombinant polypeptide can be a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence. The oil-body-

-8-

surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. Optionally, the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said sequence encoding the first recombinant polypeptide.

Also provided herein are isolated oil bodies comprising a multimericprotein-complex comprising (i) an oil-body-targeting-protein and (ii) a first recombinant polypeptide, said oil bodies further comprising a second 10 recombinant polypeptide, wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex. The oil-body-targetingprotein can be selected from an oil-body-protein or an immunoglobulin, and the oil-body-protein can be an oleosin or a caleosin. The multimeric-fusion-protein can be a heteromultimeric-fusion-protein, wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox 15 complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For 20 example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

25 Also provided herein are isolated oil bodies comprising

- (a) a first fusion protein comprising a first oil-body-targeting-protein fused to a first recombinant polypeptide; and
- (b) a second fusion protein comprising a second oil-body-targeting-protein fused to a second recombinant polypeptide,
- wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin, and the oil-body-protein can be an

-9-

oleosin or a caleosin. The multimeric-fusion-protein can be a heteromultimeric-fusion-protein, wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

10

15

20

25

30

Also provided are cells and transgenic plants comprising oil bodies, multimeric-protein-complexes, and multimeric-fusion-proteins, set forth herein. In one embodiment, the first recombinant polypeptide can be an immunoglobulinpolypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-bodytargeting-protein can comprise protein A, protein L or protein G. In embodiments, wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase, the methods described herein can be used to formulate the oil bodies for use in the preparation of a food product, personal care product or pharmaceutical composition. These formulations can further comprise the addition of NADP or NADPH. The food product can be a milk or wheat based food product. The personal care product can reduce the oxidative stress to the surface area of the human body or can be used to lighten the skin. The pharmaceutical composition can be used to treat chronic obstructive pulmonary disease (COPD), cataracts,

diabetes, envenomation, bronchiopulmonary disease, malignancies, psoriasis, reperfusion injury, wound healing, sepsis, Gl bleeding, intestinal bowel disease (IBD), ulcers, GERD (gastro esophageal reflux disease).

Also provided herein are compositions comprising isolated oil bodies, thioredoxin and thioredoxin-reductase, wherein said thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194, and said thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. The composition can further comprise NADP or NADPH. In another embodiment, the composition comprises a first recombinant polypeptide that can be an immunoglobulin-polypeptide-chain and a second recombinant polypeptide. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

10

15

20

25

30

Also provided are multimeric-fusion-proteins, wherein the fusion-protein contains two or more polypeptide chains selected from the group of proteins set forth in Figure 5. Methods are also provided of reducing allergenicity of a food comprising the steps of providing the isolated oil bodies set forth herein; and adding the isolated oil bodies to the food, whereby allergenicity of the food is reduced. The food can be selected from the group consisting of wheat flour, wheat dough, milk, cheese, yogurt and ice cream. The various methods of treating food can further comprise providing NADH as a co-factor in the substantial absence of NADPH.

Also provided herein are methods of treating or protecting a target against oxidative stress, comprising the steps of providing the recombinant redox fusion polypeptide comprising thioredoxin and thioredoxin-reductase; and contacting the recombinant fusion polypeptide with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress. The target can be selected from the group consisting of a molecule, a molecular complex, a cell, a tissue, and an organ.

Also provided herein are methods for preparing an enzymatically active redox protein associated with oil bodies comprising:

a) producing in a cell a redox fusion polypeptide comprising a first redox protein linked to a second redox protein;

5

10

15

20

25

30

- b) associating said redox fusion polypeptide with oil bodies through an oil-body-targeting-protein capable of associating with said redox fusion polypeptide and said oil bodies; and
- c) isolating said oil bodies associated with said redox fusion polypeptide. The first redox protein can be a thioredoxin and the second redox protein can be a thioredoxin-reductase.

Also, provided herein are methods of producing an immunoglobulin, said method comprising: (a) producing in a cell comprising oil bodies, a first immunoglobulin-polypeptide-chain and a second immunoglobulin-polypeptide-chain wherein said first immunoglobulin-polypeptide-chain is capable of associating with said second immunoglobulin-polypeptide-chain to form said immunoglobulin; and (b) associating said immunoglobulin with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said first immunoglobulin-polypeptide-chain. For example, the first immunoglobulin-polypeptide-chain can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second immunoglobulin-polypeptide-chain can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

· Also provided herein are methods for preparing a redox protein or an immunoglobulin associated with oil bodies comprising:

- a) introducing into a cell a chimeric nucleic acid sequence comprising:
  - 1) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
  - 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a

-12-

nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein, or a nucleic acid sequence encoding a immunoglobulin comprising a first immunoglobulin-polypeptide-chain linked to a second immunoglobulin-polypeptide-chain, operatively linked to;

- 3) a third nucleic acid sequence capable of terminating transcription in said cell;
- b) growing said cell under conditions to permit expression of said redox fusion polypeptide or immunoglobulin in a progeny cell comprising oil bodies; and

5

10

20

25

30

c) isolating from said progeny cell said oil bodies comprising said redox fusion polypeptide or immunoglobulin. In certain embodiments, positioned between said nucleic acid sequence encoding a sufficient portion of an oil-bodyprotein and said nucleic acid sequence encoding a redox fusion polypeptide or immunoglobulin can be a linker nucleic acid sequence encoding an oil-bodysurface-avoiding linker amino acid sequence. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged or have a molecular weight of at least 35 kd. Optionally, the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said nucleic acid sequence encoding a redox fusion polypeptide. In this optional embodiment, also contemplated is the introduction of an enzyme or chemical that cleaves said redox fusion polypeptide from said oil body, thereby obtaining isolated redox fusion polypeptide. The first redox protein can be a thioredoxin and said second redox protein can be a thioredoxin-reductase. In one embodiment, the thioredoxin and thioredoxin-reductase can be obtained from Arabidopsis. In another embodiment, the first redox protein is at least 5 times more active when produced as a redox fusion polypeptide as compared to the production of the first redox protein without the second redox protein.

Also provided herein, for use with the various methods set forth herein is the formulation of an emulsion of the oil bodies associated with the redox fusion polypeptide for use in the preparation of a product capable of treating oxidative stress in a target, a product capable of chemically reducing a target, pharmaceutical composition, a personal care product or a food product.

Accordingly, an emulsion formulation composition is provided.

Also provided herein is a chimeric nucleic acid comprising:

5

15

20

25

30

- 1) a first nucleic acid sequence capable of regulating transcription in a host cell operatively linked to;
- 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
- a third nucleic acid sequence capable of terminating transcription in said cell. The oil-body-protein can be an oleosin or a caleosin, the first redox protein can be a thioredoxin and said second redox protein can be a thioredoxin-reductase. In certain embodiments, positioned between said nucleic acid sequence encoding a sufficient portion of an oil-body-protein and said nucleic acid sequence encoding a redox fusion polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. In one embodiment, the gene fusion optionally further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said nucleic acid sequence encoding a redox fusion polypeptide.

Also provided herein are transgenic plants, e.g., safflower plants, comprising any of the chimeric nucleic acid sequences and constructs described herein. The chimeric nucleic acids can be contained within a plastid.

Accordingly, isolated plastids are provided having chimeric nucleic acids therein.

-14-

Also provided are plant seeds comprising the chimeric nucleic acids provided herein.

Also provided are oil body preparations obtained using any of the methods provided herein, and food products, pharmaceutical compositions, and personal care products containing the oil body preparations. The products and/or compositions provided herein are capable of treating oxidative stress in a target, capable of chemically reducing a target. Also provided is a detergent composition comprising an oil body preparation capable of chemically reducing a target, and related methods of cleansing an item, comprising administering such product to the item under conditions that promote cleansing.

10

15

20

25

30

Also provided herein are nucleic acid constructs comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one thioredoxin-related protein or an active fragment thereof. In one embodiment, the at least one thioredoxin-related protein can be thioredoxin. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194. The thioredoxin can be obtained from *Arabidopsis* or wheat.

In another embodiment, the at least one thioredoxin-related protein can be thioredoxin-reductase. The thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313 and/or derived from *Arabidopsis* or wheat. The thioredoxin-reductase can be an NADPH-dependent thioredoxin-reductase. The second region can encode a thioredoxin and thioredoxin-reductase. In one embodiment, the thioredoxin and thioredoxin-reductase is obtained from *Mycobacterium leprae*. In another embodiment, the at least one thioredoxin-related protein can be an engineered fusion protein. The first region can precede, in a 5' to 3' direction, the second region. Alternatively, the first region follows, in a 5' to 3' direction, the second region. The gene fusion can optionally further comprise a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both. A seed-specific promoter, such as a phaseolin promoter, can be operably linked to

the gene fusion. In one embodiment, at least one thioredoxin-related protein is derived from a plant species selected from the group consisting of *Arabidopsis* and wheat. In another embodiment, at least one thioredoxin-related protein can be derived from *E. coli*.

5

10

15

20

25

30

In one embodiment, the gene fusion further comprises a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the linker amino acid sequence is positioned between the first region and the second region. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. In addition, the gene fusion can further comprise a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and the second region.

Also provided herein are transgenic plants containing a nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof. The thioredoxin-related protein can be thioredoxin. The nucleic acid construct can be contained within a plastid. In one embodiment, when the first thioredoxin-related protein is thioredoxin and the construct can further comprise a region encoding a thioredoxin-reductase. The gene fusion can optionally further comprise a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both. The gene fusion can optionally further comprise a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the nucleic acid encoding the linker amino acid sequence is positioned between the region encoding an oil-body-protein and the region encoding a first thioredoxin-related protein. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. The gene fusion can optionally further comprise a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is

positioned between the oil-body-surface-avoiding linker amino acid sequence and the region encoding a first thioredoxin-related protein.

Also provided is a transgenic plant comprising a nucleic acid construct, a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, wherein a fusion protein comprising activities of oleosin and the thioredoxin-related protein is produced in a seed of the plant. In another embodiment, a thioredoxin-related protein having concentration of at least about 0.5% of total cellular seed protein is provided. Also provided herein is an extract comprising an activity of a thioredoxin-related protein. Also provided are oil bodies and/or oil obtained from various seeds.

Also provided herein are methods of making a fusion protein comprising a thioredoxin-related activity, the method comprising the steps of:

- a) providing a transgenic plant comprising a nucleic acid construct comprising a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, the gene fusion encoding a fusion protein comprising a thioredoxin-related activity;
  - b) obtaining seeds from the plant; and

10

15

20

25

30

- c) recovering the fusion protein by isolating oil bodies from the seeds. In one embodiment, the oil bodies are fractionated to achieve partial purification of the fusion protein. The oil bodies can be in association with a fusion protein.
- The oil-body-protein can be cleaved from the thioredoxin-related protein after fractionation of the oil bodies. The cleaving step can make use of a protease or chemical proteolysis.

Also provided herein are methods of reducing allergenicity of a food comprising the steps of:

a) providing a preparation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

5

10

15

20

25

30

b) adding the preparation to the food, whereby allergenicity of the food is reduced due to activity of the thioredoxin-related protein or fragment. The food can be wheat flour, wheat dough, milk, cheese, yogurt and ice cream. In one embodiment, NADH is used as a co-factor in the substantial absence of NADPH.

Also provided herein are pharmaceutical compositions comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier. The oil bodies can be associated with the fusion protein. Also provided is a cosmetic formulation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier. Also provided are methods of treating or protecting a target against oxidative stress, comprising the steps of:

a) providing a preparation comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

b) contacting the preparation with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress. The target can be selected from the group consisting of a molecular complex, a cell, a tissue, and an organ.

Also provided is a nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one polypeptide or an active fragment thereof, and an oil-body-surface-avoiding linker in frame between the first and second region polypeptides. Also provided are methods of expressing this construct into the encoded amino acid sequence; and oil bodies, formulations, emulsions, cells, and plants comprising the construct and encoded amino acid sequence. These particular constructs, oil bodies, formulations, emulsions, cells, and plants can be produced according to the methods described herein. The second region can encode any polypeptide, for example, a therapeutically, nutritionally, industrially or cosmetically useful

10

15

20

25

peptide as set forth herein. For example, the second region can encode a redox protein, an immunoglobulin, a thioredoxin-related protein or any one or more recombinant polypeptides of a multimeric-protein-complex.

Other features and advantages of the present invention will become

readily apparent from the following detailed description. It should be understood however that the detailed description and the specific examples while indicating particular embodiments of the invention are given by way of illustration only.

### **BRIEF DESCRIPTION OF THE DRAWINGS**

Figure 1 shows a ClustalW Formatted Alignment comparison of the published NADPH thioredoxin-reductase nucleic acid sequence (SEQ ID NO:9) (ATTHIREDB-Jacquot et al. J. Mol. Biol. (1994) 235 (4):1357-63.) with the sequence isolated herein in Example 1 (TR; SEQ ID NO:8).

Figure 2 shows a ClustalW Formatted Alignment comparison of the deduced amino acid sequence of the published NADPH thioredoxin-reductase sequence (SEQ ID NO:12)(ATTHIREDB Jacquot et al. J. Mol. Biol. (1994) 235 (4):1357-63.) with the sequence isolated herein in Example 1 (TR; SEQ ID NO:13).

Figure 3 shows a clustal alignment comparing the amino acid sequence of the *Arabidopsis thaliana* thioredoxin-reductase-linker-thioredoxin synthetic fusion (Arab TR-link-Trxh; SEQ ID NO:37) to the *Mycobacterium leprae* thioredoxin-reductase-thioredoxin natural fusion (M.lep TR/Trxh; SEQ ID NO:36) natural fusion. Overall, the proteins are approximately 50% identical at the amino acid level.

Figure 4 is a bar graph showing the thioredoxin/thioredoxin-reductase activity measurements for the various transgenic *Arabidopsis* seed fractions. Relative specific activity is expressed as a percentage of the *E. coli* thioredoxin and thioredoxin-reductase activities. The numbered bars in the graph correspond to the following:

- 30 1. W.T. + oleosin-thioredoxin
  - 2. W.T. + thioredoxin-oleosin
  - 3. W.T. + thioredoxin

-19-

- 4. W.T. + oleosin-thioredoxin-reductase
- 5. W.T. + thioredoxin-reductase-oleosin
- 6. W.T. + thioredoxin-reductase
- 7. thioredoxin + oleosin-thioredoxin-reductase
- 5 8. thioredoxin + thioredoxin-reductase-oleosin
  - 9. thioredoxin + thioredoxin-reductase
  - 10. thioredoxin-reductase + oleosin-thioredoxin
  - 11. thioredoxin-reductase + thioredoxin-oleosin
  - 12. oleosin-M.lep TR/Trxh
- 10 13. E. coli thioredoxin-reductase + thioredoxin

Figure 5 provides a listing of exemplary proteins for use in the heteromultimeric-fusion-proteins and heteromultimeric-protein-complexes provided herein.

#### **DETAILED DESCRIPTION**

25

30

- As hereinbefore mentioned, the present invention relates to novel and improved methods for the production of multimeric proteins, including a first and second recombinant polypeptide, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulin-polypeptide-chains, immunoglobulins, redox-fusion-polypeptides, and a first and second thioredoxin-related protein; and related products. These methods permit the production of
  - active multimeric-protein-complexes in association with oil bodies. The oil bodies in association with the multimeric-protein-complex may be used to prepare various useful emulsions.
  - Accordingly, provided herein are methods of producing a recombinant multimeric-protein-complex associated with an oil body, said method comprising:
  - (a) producing in a cell comprising oil bodies, a first recombinant polypeptide and a second recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said second recombinant polypeptide in the cell to form said multimeric-protein-complex; and

-20-

(b) associating said multimeric-protein-complex with an oil body through an oil-body-targeting-protein capable of associating with said oil body and said first recombinant polypeptide.

#### **Definitions and terms**

5

10

20

25

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this invention belongs. Where permitted, all patents, applications, published applications and other publications and sequences from GenBank, SwissPro and other data bases referred to throughout in the disclosure herein are incorporated by reference in their entirety.

As used herein, the phrase "multimeric-protein-complex", refers to two or more polypeptide chains that permanently or repeatedly interact or permanently or repeatedly coordinate to form a biologically active assembly comprising said two or more polypeptide chains. It should be noted that the polypeptides may be independently biologically active without interaction or coordination to form the complex. The multimeric-protein-complex may provide a biological structure, or it may be capable of facilitating a chemical or biological reaction. For example, one of the protein regions within the multimeric-protein-complex can repeatedly activate or repeatedly inactivate the biological or metabolic activity of one or more of the other proteins contained within the multimeric-protein-complex. In one embodiment, the first and second recombinant polypeptide contained in a multimeric-protein-complex may either associate or interact as independent non-contiguous polypeptide chains or the multimeric-protein-complex may be prepared as a fusion polypeptide (multimeric-fusion-protein) between the first and second recombinant polypeptide.

One example of a repeated (e.g., reoccurring) interaction or association between the two or more polypeptides of a multimeric-protein-complex provided herein is the interaction between two or more non-identical redox proteins to form a heteromultimeric-protein-complex. Exemplary redox proteins for use in this regard are thioredoxin and the thioredoxin-reductase. A further example is the interaction between two or more immunoglobulin-polypeptide-chains to form an immunoglobulin. As used herein, the phrase "heteromultimeric-protein-

complex", refers to two or more non-identical polypeptide chains that permanently or repeatedly interact or permanently or repeatedly coordinate to form a biologically active assembly comprising said two or more polypeptide chains. Other examples of multimeric-protein-complexes provided herein include a first and second recombinant polypeptide, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, first and second immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and a first and second thioredoxin-related protein.

The recombinant polypeptide or multimeric-protein-complex is associated with an oil body. As used herein, the phrase "oil body" or "oil bodies" refers to any oil or fat storage organelle in any cell type. Accordingly, the oil bodies may be obtained from any cell comprising oil bodies, including plant cells (described in for example: Huang (1992) Ann. Rev. Plant Mol. Biol. 43: 177-200), animal cells (described in for example: Murphy (1990) Prog Lipid Res 29(4): 299-324), including adipocytes, hepatocytes, steroidogenic cells, mammary epithelial cells, macrophages, algae cells (described in for example: Rossler (1988) J. Physiol. London, 24: 394-400) fungal cells, including yeast cells (described in for example Leber et al. (1994) Yeast 10: 1421-1428) and bacterial cells (described in for example: Pieper-Furst et al. (1994) J. Bacteriol. 176: 4328-4337). Preferably the oil bodies used herein are oil bodies obtainable from plant cells and more preferably the oil bodies obtainable from plant seed cells.

10

20

30

As used herein, the phrase "is capable of associating with", "associate" or grammatical variations thereof, refers to any interaction between two or more polypeptides, including any covalent interactions (e.g. multimeric-fusion-proteins) as well as non-covalent interactions. Exemplary non-covalent interactions can be between the oil-body-targeting-protein and a redox protein or immunoglobulin-polypeptide-chain, as well as between two or more different proteins contained within two or more separate oil-body-protein fusion proteins (e.g., the redox proteins in oleosin-thioredoxin and oleosin-thioredoxin-reductase).

As used herein, the term "recombinant" (also referred to as heterologous) in the context of recombinant proteins and amino acids, means "of different natural origin" or represents a non-natural state. For example, if a host cell is

PCT/US01/50240 WO 02/50289

transformed with a nucleotide sequence derived from another organism, particularly from another species, that nucleotide sequence and amino acid sequence encoded thereby, is recombinant (heterologous) with respect to that host cell and also with respect to descendants of the host cell which carry that 5 gene. Similarly, recombinant (or heterologous) refers to a nucleotide sequence derived from and inserted into the same natural, original cell type, but which is present in a non-natural state, e.g., a different copy number, or under the control of different regulatory elements. A transforming nucleotide sequence may include a recombinant coding sequence, or recombinant regulatory elements. Alternatively, the transforming nucleotide sequence may be completely heterologous or may include any possible combination of heterologous and endogenous nucleic acid sequences.

10

20

25

30

In various embodiments of the present invention, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins, are produced in a cell comprising oil bodies. As used herein the phrase "in a cell", "in the cell", or grammatical variations thereof, mean that the first and/or second recombinant polypeptides, multimericprotein-complexes, heteromultimeric-protein-complexes, multimeric-fusionproteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulinpolypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins, may be produced in any cellular compartment of that cell, so long as that cell comprises oil bodies therein. In embodiments of the invention in which plant cells are used, the phrase is intended to include the plant apoplast.

In various embodiments provided herein, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and thioredoxin-related proteins, associate with an oil body through an oil-bodytargeting-protein. As used herein, the phrase "oil-body-targeting-protein" refers to any protein, protein fragment or peptide capable of associating with an oil

20

30

body. Exemplary oil-body-targeting-proteins for use herein include oil-bodyproteins, such as oleosin and caleosin; immunoglobulins, such as bi-specific antibodies; and the like.

In embodiments described herein in which an oil-body-protein is used, the
first and/or second recombinant polypeptides, multimeric-protein-complexes,
heteromultimeric-protein-complexes, multimeric-fusion-proteins,
heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, and thioredoxin-related proteins, are
preferably fused to the oil-body-protein. The term "oil-body-protein" refers to
any protein naturally present in cells and having the capability of association
with oil bodies, including any oleosin or caleosin.

Accordingly, provided herein a method of expressing a recombinant multimeric-protein-complex comprising a first and second recombinant polypeptide in a cell, said method comprising:

- 15 (a) introducing into a cell a first chimeric nucleic acid sequence comprising:
  - (i) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
  - (ii) a second nucleic acid sequence encoding a first recombinant polypeptide, such as a redox protein, an immunoglobulin-polypeptide-chain or an thioredoxin-related protein, fused to an oil-body-protein;
  - (b) introducing into said cell a second chimeric nucleic acid sequence comprising:
  - (i) a third nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
- (ii) a fourth nucleic acid sequence encoding a second recombinant polypeptide,
   such as a second redox protein, a second immunoglobulin-polypeptide-chain or a second thioredoxin-related protein,;
  - (c) growing said cell under conditions to permit expression of said first and second recombinant polypeptide in a progeny cell comprising oil bodies wherein said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimeric-protein-complex, preferably in said progeny cell; and

(d) associating said first recombinant polypeptide with an oil body through said oil-body-protein.

The term "nucleic acid" as used herein refers to a sequence of nucleotide or nucleoside monomers consisting of naturally occurring bases, sugars and intersugar (backbone) linkages. The term also includes modified or substituted sequences comprising non-naturally occurring monomers or portions thereof. which function similarly. The nucleic acid sequences may be ribonucleic acids (RNA) or deoxyribonucleic acids (DNA) and may contain naturally occurring bases including adenine, guanine, cytosine, thymidine and uracil. The sequences also may contain modified bases such as xanthine, hypoxanthine, 2aminoadenine, 6-methyl, 2-propyl and other alkyl adenines, 5-halo-uracil, 5-halo cytosine, 6-aza uracil, 6-aza cytosine and 6-aza thymine, pseudo uracil, 4thiouracil, 8-halo adenine, 8-amino adenine, 8-thiol-adenine, 8-thio-alkyl adenines, 8-hydroxyl adenine and other 8-substituted adenines, 8-halo guanines, 8 amino guanine, 8 thiol guanine, 8-thioalkyl guanines, 8 hydroxyl guanine and other 8-substituted guanines, other aza and deaza uracils, thymidines, cytosines, adenines, or guanines, 5-trifluoromethyl uracil and 5-trifluoro cytosine. Multimeric-protein-complexes

10

20

25

30

In accordance with the methods and compositions provided herein, any two recombinant polypeptides capable of forming a multimeric-protein-complex may be used. The nucleic acid sequences encoding the two recombinant polypeptides may be obtained from any biological source or may be prepared synthetically. In general nucleic acid sequence encoding multimeric proteins are known to the art and readily available. Known nucleic acid sequences encoding multimeric-protein-complexes may be used to design and construct nucleic acid sequence based probes in order to uncover and identify previously undiscovered nucleic acid sequences encoding multimeric-protein-complexes, for example, by screening cDNA or genomic libraries or using 2- or multi-hybrid systems. Thus, additional nucleic acid sequences encoding multimeric-protein-complexes may be discovered and used as described herein.

The first and/or second recombinant polypeptides that are comprised within a multimeric-protein-complex provided herein, can themselves be in the

form of heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein.

The nucleic acid sequence encoding the first and second recombinant polypeptide, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein may be obtained from separate sources or may be obtained from the same source. In general however, such nucleic acid sequence is obtained from the same or a similar biological source. In certain embodiments wherein the nucleic acid sequence encoding the first and second recombinant polypeptide protein are obtained from the same source, the nucleic acid sequence encoding the first recombinant polypeptide and second recombinant polypeptide may be naturally fused. In accordance with a particular embodiment, the nucleic acid sequences encoding the first and second recombinant polypeptide are obtained from a plant source.

### Oil-Body-Surface-Avoiding Linkers

5

10

15

Polypeptide spacers or linkers of variable length and/or negative charge 20 can be used herein to separate the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimericfusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and the first and/or second thioredoxin-related proteins from the in-frame oil-body-targeting-25 protein, to improve activity of and/or the accessibility of the polypeptide or complex. For example, in one embodiment set forth herein, positioned between a nucleic acid sequence encoding a sufficient portion of an oil-body-protein and a nucleic acid sequence encoding either the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, 30 multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and the first

and/or second thioredoxin-related proteins; is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.

Oil-body-surface-avoiding linkers are positioned between the oil-body targeting sequence and an in-frame recombinant polypeptide of interest, e.g., the multimeric-protein-complexes provided herein, serve to increase the distance and or decrease the interaction between the negatively charged oil body surface and the recombinant polypeptide of interest. A negatively charged linker is repelled by the negatively charged oil body surface, in turn increasing the distance or decreasing the interaction of its attached recombinant polypeptide with the oil body surface. As a consequence of the increased distance from the oil body surface, the recombinant polypeptide will be more accessible, e.g. to its target(s) substrate, protein substrate, protein partner, and less affected by the charged oil body surface. Exemplary linker sequences for use herein can be either a negatively charged linker, or a linker having a molecular weight of at least about 35 kd or more.

10

15

20

25

30

As used herein, a "negatively charged linker" sequence, refers to any amino acid segment, or nucleic acid encoding such, that has a pl less than or equal to the pl of an oil body. In certain embodiments, the pl of the negatively charged linker is about 90%, 80%, 70%, 60%, 50%, 40%, 30%, down to about 25% or more, below that of the plof an oil body in the particular plant or cell system being used. Exemplary negatively charged linkers can be prepared comprising any combination of the negatively charged amino acid residues. For example, in one embodiment, a negatively charged linker comprises either a poly-glutamate or poly-aspartate sequence, or any combination of both amino acid residues. The negatively charged linker is typically at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more amino acids in length. The negatively charged linkers are preferably non-proteolytic (e.g., non-proteolytic linkers), having no site for efficient proteolysis. When linker size rather than charge is used to minimize interaction of the recombinant polypeptide of interest with the oil body surface, then the linker is nonproteolytic and ranges in molecular weight from about 35 kd up to about 100 kd. The upper size limit is chosen such that the expression of, the activity of,

the conformation of, and/or the access to target of, the recombinant polypeptide of interest is not significantly affected by the linker.

In certain embodiments, described herein where a non-proteolytic linker amino acid sequence is employed, the gene fusion or protein fusion (multimeric-5 fusion-protein) can optionally further comprise a linker nucleic or amino acid sequence encoding a sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the non-proteolytic linker sequence and sequence encoding the desired recombinant protein region, e.g., the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins set forth herein. When a cleavable linker sequence is used herein, in a particular embodiment, it is further downstream than the non-proteolytic linker sequence from the oil-body-targeting-protein region of the fusion protein. By virtue of cleavable linker, the recombinant fusion polypeptides provided herein, such as the multimeric-fusion-proteins and redox fusion polypeptides, can be isolated and purified by introducing an enzyme or chemical that cleaves said multimeric-fusion-protein and/or redox fusion polypeptide from said oil body, thereby obtaining and/or isolating the desired protein. It is contemplated herein that the use of cleavable linker sequence downstream of the non-proteolytic linker/spacer sequence will improve the yield of protein recovery when isolating or purifying proteins using the methods provided herein.

15

20

25

30

The nucleic acid sequences encoding the first or second recombinant polypeptide may be altered to improve expression levels for example, by optimizing the nucleic acids sequence in accordance with the preferred codon usage for the particular cell type which is selected for expression of the first and second recombinant polypeptide, or by altering of motifs known to destabilize mRNAs (see for example: PCT Patent Application 97/02352). Comparison of the codon usage of the first and second recombinant polypeptide with codon usage of the host will enable the identification of codons that may be changed. For example, typically plant evolution has tended towards a preference for CG

-28-

rich nucleotide sequences while bacterial evolution has resulted in bias towards AT rich nucleotide sequences. By modifying the nucleic acid sequences to incorporate nucleic acid sequences preferred by the host cell, expression may be optimized. Construction of synthetic genes by altering codon usage is described in for example PCT patent Application 93/07278. The first and second recombinant polypeptide can be altered using for example targeted mutagenesis, random mutagenesis (Shiraishi et al. (1998) Arch. Biochem. Biophys. 358: 104-115; Galkin et al. (1997) Protein Eng. 10: 687-690; Carugo et al. (1997) Proteins 28: 10-28; Hurley et al. (1996) Biochemistry 35: 5670-5678), gene shuffling, and/or by the addition of organic solvent (Holmberg et al. (1999) Protein Eng. 12: 851-856). Any polypeptide spacers that are used in accordance with the methods and products provided herein may be altered in similar ways.

In particular embodiments provided herein, the recombinant polypeptides or thioredoxin-related proteins capable of forming a multimeric-protein-complex are capable of forming a heteromultimeric-protein-complex. Examples of heteromultimeric-protein-complexes that contain polypeptide chains that repeatedly interact, either to activate, inactivate, oxidize, reduce, stabilize, etc., with one another, that can be produced in association with oil bodies using the methods provided herein include those set forth in Figure 5. Accordingly, exemplary proteins for use in the heteromultimeric-protein-complexes and nucleic acid constructs encoding such, provided herein include, among others described herein, those set forth in Figure 5.

Other polypeptide regions that can be used in the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, provided herein include, among other, those immunoglobulin regions set forth in Table 1.

10

15

20

25

-29-

### **TABLE 1 - ANTIBODY HETERODIMERS**

|    | Class or molecule   | <u>Subunits</u>   |
|----|---|---|
|    | Fab   | Variable region and first constant region of                                  |
|    |   | heavy chain and complete light chain  |
| 5  | <b>Fv</b>   | Variable regions of heavy and light antibody chains                           |
|    | IgA   | heavy chains, light chains and J (joining) chain                              |
|    | IgG, IgD, IgE   | heavy and light chains  |
|    | lgM   | heavy chains, light chains and J (joining) chain                              |
|    | Antibody chain(s) and a toxin   | Antibody chain(s) and a toxin   |
| 10 | Autoantigens, allergens and<br>transplant antigens with an<br>adjuvant or tolerogen | Autoantigens, allergens and transplant antigens with an adjuvant or tolerogen |
|    | Chimeras using antibody Fc domain   | Receptor subunits fused to the constant region of antibody heavy chains       |
| 15 |   |   |

As set forth above, in one embodiment, exemplary heteromultimericprotein-complexes and exemplary heteromultimeric-fusion-proteins provided herein comprise redox proteins, such as the thioredoxins and thioredoxinreductases and immunoglobulins.

20

25

30

35

### Oil-body-targeting-proteins

The nucleic acid sequence encoding the oil-body-targeting-protein that may be used in the methods and compositions provided herein may be any nucleic acid sequence encoding an oil-body-targeting-protein, protein fragment or peptide capable of association with first recombinant polypeptide, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein and the oil bodies. The nucleic acid sequence encoding the oil body targeting peptide may be synthesized or obtained from any biological source.

For example, in one embodiment the oil-body-targeting-protein is an immunoglobulin or an immunoglobulin derived molecule, for example, a bispecific single chain antibody. The generation of single chain antibodies and bi-specific single chain antibodies is known to the art (see, e.g., US Patents US 5,763,733,

US5,767,260 and US5,260,203). Nucleic acid sequences encoding single chain antibodies functioning as oil-body-targeting-proteins may be prepared from hybridoma cell lines expressing monoclonal antibodies raised against an oleosin as described by Alting-Mees et al (2000) IBC's Annual International Conference on Antibody Engineering, Poster #1. In order to attain specificity for the first recombinant polypeptide a nucleic acid sequence encoding a second single chain antibody prepared from a monoclonal raised against the first recombinant polypeptide may be prepared and linked to the anti-oleosin single chain antibody. In this embodiment the oil body associates with the first recombinant polypeptide through non-covalent interactions of the oil-body-targeting-protein with the first recombinant polypeptide and the oil body. Alternatively the first recombinant polypeptide may be prepared as a fusion protein with an oil-body-targeting-protein. For example, a nucleic acid sequence encoding a single chain antibody raised against an oleosin may be fused to a nucleic acid sequence encoding the first recombinant polypeptide

10

15

20

30

Non-immunoglobulin-based oil-body-targeting-proteins capable of association with the first recombinant polypeptide may be discovered and prepared using for example phage display techniques (Pharmacia Biotech Catalogue Number 27-9401-011 Recombinant Phage Antibody System Expression Kit).

Oil-body-targeting-proteins may also be chemically modified. For example, oleosins may be modified by changing chemical modification of the lysine residues using chemical agents such as biotinyl-N-hydroxysuccinimide ester resulting in a process referred to as biotinylation. Conveniently this is accomplished by *in vitro* biotinylation of the oil bodies. *In vivo* biotinylation may be accomplished using the biotinylation domain peptide from the biotin carboxy carrier protein of *E. coli* acetyl-CoA carboxylase (Smith et al. (1998) Nucl. Acids. Res. 26: 1414-1420). Avidin or streptavidin may subsequently be used to accomplish association of the redox protein with the oil body.

In a particular embodiment the oil-body-targeting-protein is an oil-bodyprotein such as for example an oleosin or a caleosin or a sufficient portion derived thereof capable of targeting to an oil body. Nucleic acid sequences

-31-

encoding oleosins are known to the art. These include for example the Arabidopsis oleosin (van Rooijen et al (1991) Plant Mol. Bio. 18:1177-1179); the maize oleosin (Qu and Huang (1990) J. Biol. Chem. Vol. 265 4:2238-2243); rapeseed oleosin (Lee and Huang (1991) Plant Physiol. 96:1395-1397); and the 5 carrot oleosin (Hatzopoulos et al (1990) Plant Cell Vol. 2, 457-467.). Caleosin nucleic acid sequences are also known to the art (Naested et al (2000) Plant Mol Biol. 44(4):463-476; Chen et al (1999) Plant Cell Physiol. 40(10):1079-1086). Animal cell derived oil body proteins that may be used herein include adopihilin (Brasaemle et al, (1997) J. Lipid Res., 38: 2249-2263; Heid et al. (1998) Cell Tissue Research 294: 309-321), perilipin (Blanchette-Mackie et al. (1995), J. Lipid Res. 36: 1211-1226; Servetnick et al. (1995) J. Biol. Chem. 270: 16970-16973), apolipoproteins such as apo A-I, A-II, A-IV, C-I, C-II, CIII (Segrest et al. (1990), Proteins 8:103-117) and apoB (Chatterton et al. (1995) J. Lipid Res. 36: 2027-2037; Davis, RA in: Vance DE, Vance J. editors. Lipoprotein structure and secretion. The Netherlands, Elsevier, 191: 403-426.

10

15

25

30

In one embodiment, the first recombinant polypeptide is fused to an oilbody-protein. The methodology is further described in US patent 5,650,554, which is incorporated herein by reference in its entirety. The first recombinant polypeptide may be fused to the N-terminus as well as to the C-terminus of the oil-body-protein (as described in: Moloney and van Rooijen (1996) INFORM 7:107-113) and fragments of the oil-body-protein such as for example the central domain of an oleosin molecule, or modified versions of the oil-bodyprotein may be used. In this embodiment, the second recombinant polypeptide is expressed intracellularly and then intracellularly associates with the first recombinant polypeptide to form the multimeric-protein-complex in the cell. Oil bodies comprising the multimeric-protein-complex are then conveniently isolated from the cells.

In a further embodiment both the first and second recombinant polypeptide are separately fused to an oil-body-protein. In this embodiment nucleic acid sequences encoding the first and second polypeptides may be prepared separately and introduced in separate cell lines or they may be introduced in the same cell lines. Where the nucleic acid sequences are

introduced in the same cell line, these nucleic acid sequence may be prepared using two separate expression vectors, or they may be prepared using a single vector comprising nucleic acid sequences encoding both the first polypeptide fused to an oil body protein and the second polypeptide fused to an oil-body-protein. Where separate cell lines are used subsequent mating of the offspring (e.g., mating of plants) is used to prepare a generation of cells comprising oil bodies which comprise both the first and second recombinant polypeptide fused to an oil-body-protein.

In further alternate embodiment, the first and second recombinant polypeptide are fused to form a multimeric-fusion-protein comprising the multimeric-protein-complex. In such an embodiment, the first and second polypeptide is associated with the oil body through an oil-body-targeting-protein capable of associating with both the fusion protein and with the oil body. In a particular embodiment, the fusion protein comprising the multimeric-protein-complex is fused to an oil-body-protein, for example, an oleosin or caleosin.

10

15

20

25

30

In embodiments provided herein in which the multimeric-protein-complex is an immunoglobulin (e.g., a multimeric-immunoglobulin-complex), a particularly preferred oil body targeting protein is an oleosin or caleosin associated with an immunoglobulin binding protein, such as for example protein A (US Patent 5,151,350), protein L (US Patent 5,965,390) and protein G (US Patent 4,954,618), or active fragments of such immunoglobulin binding proteins.

New oil-body-proteins may be discovered for example by preparing oil bodies (described in further detail below) and identifying proteins in these preparations using for example SDS gel electrophoresis. Polyclonal antibodies may be raised against these proteins and used to screen cDNA libraries in order to identify nucleic acid sequences encoding oil-body-proteins. The methodologies are familiar to the skilled artisan (Huynh et al. (1985) in DNA Cloning Vol. 1. a Practical Approach ed. DM Glover, IRL Press, pp 49-78). New oil-body-proteins may further be discovered using known nucleic acid sequences encoding oil-body-proteins (e.g. the *Arabidopsis*, rapeseed, carrot and corn nucleic acid sequences) to probe for example cDNA and genomic libraries for the presence of nucleic acid sequences encoding oil-body-proteins.

In one embodiment, the first and second polypeptide are a first and second redox protein. Accordingly, one embodiment provided herein relates to novel and improved methods for the production of redox proteins. It has unexpectedly been found that a redox protein when prepared as a fusion protein with a second redox protein is fully enzymatically active when produced in association with an oil body. In contrast, when the redox protein is prepared without the second redox protein it has reduced enzymatic activity. In one embodiment, the first redox protein is at least 5 times more active when produced as a redox fusion polypeptide relative to production as a non-fusion polypeptide.

Accordingly, provided herein are methods for producing an oil body associated with a heteromultimeric redox protein complex, said method comprising:

10

15

20

- (a) producing in a cell comprising oil bodies, a first redox protein and a second redox protein wherein said first redox protein is capable of interacting with said second redox protein, preferably in the cell, to form said heteromultimeric redox protein complex; and
- (b) associating said heteromultimeric redox protein complex with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said heteromultimeric redox protein complex.

In a particular embodiment the first and second redox protein are prepared as a fusion protein to form a redox fusion polypeptide. Accordingly, provided herein are methods for preparing an enzymatically active redox protein associated with oil bodies comprising:

- a) producing in a cell a redox fusion polypeptide comprising a first redox protein linked to a second redox protein;
  - b) associating said redox fusion polypeptide with oil bodies through an oil-body-targeting-protein capable of associating with said redox fusion polypeptide and said oil bodies; and
- 30 c) isolating said oil bodies associated with said redox fusion polypeptide.

  The oil bodies in association with the redox protein may be used to prepare a variety of useful emulsions.

As used herein the phrase "redox proteins" or grammatical variations thereof, refers to any protein or active protein fragment capable of participating in electron transport. For example, redox proteins are capable of catalyzing the transfer of an electron from an electron donor (also frequently referred to as the reducing agent) to an electron acceptor (also frequently referred to as the oxidizing agent). In the process of electron transfer, the reducing agent (electron donor) is oxidized and the oxidizing agent (electron acceptor) is reduced. Exemplary redox proteins for use herein include iron-sulfur proteins, cytochromes, redox active thiol proteins and redox-active flavoproteins. To carry out their function as conduits for electrons, redox proteins, such as thioredoxin and thioredoxin-reductase for example, are known to function by interacting or associating with one another in multimeric-protein-complexes (e.g., heteromultimeric-protein-complexes).

10

15

20

25

30

The term "redox fusion polypeptide" as used herein refers to any fusion polypeptide comprising a first redox protein linked to a second redox protein (e.g., an in-frame translational fusion). The redox proteins that may be used with the methods and compositions provided herein may be any redox protein. In one embodiment the first and second redox proteins are a pair of redox proteins that would normally occur together from the same source, in nature. In a particular embodiment, the first redox protein is a thioredoxin and the second redox protein is a thioredoxin-reductase.

The redox fusion polypeptide may be produced in any cell comprising oil bodies, including any animal cell, plant cell, algae cell, fungal cell or bacterial cell. In certain embodiments the redox fusion polypeptide is produced in a plant cell and in particular embodiments the redox fusion polypeptide is produced in the seed cells of a seed plant.

In particular embodiments the oil-body-targeting-protein that is used is an oil-body-protein. In embodiments of the present invention in which an oil-body-protein is used, the first and second redox protein are preferably covalently fused to the oil-body-protein. Accordingly, provided herein are methods for the preparation of a redox protein in association with an oil body comprising:

a) introducing into a cell a chimeric nucleic acid sequence comprising:

- a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
- a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a first nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked in reading frame to (ii) a second nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
- a third nucleic acid sequence capable of terminating transcription in said cell;
  - growing said cell under conditions to permit expression of said redox fusion polypeptide in a progeny cell comprising oil bodies;
     and
- 15 c) isolating said oil bodies comprising said redox fusion polypeptide from said progeny cell.

## **Redox Proteins**

5

In accordance with various methods and compositions provided herein, 20 any nucleic acid sequence encoding a redox protein may be used. The nucleic acid sequence encoding the first and/or second redox protein may be obtained from any biological source or may be prepared synthetically. In general, nucleic acid sequences encoding redox proteins are well known in the art and readily available. See, for example: Cristiano et al. (1993) Genomics 17: (2) 348-354, Doyama et al. (1998) Plant Sci. 137: 53-62, Hoeoeg et al. (1984) Biosci. Rep. 4: 25 917-923; as well as the Swiss Protein sequences set forth in Table 5. Known nucleic acid sequences encoding redox proteins may be used to design and construct nucleic acid sequence based probes in order to uncover and identify previously undiscovered nucleic acid sequences encoding redox proteins, for example by screening cDNA or genomic libraries. Thus, additional nucleic acid 30 sequences may be discovered and used in accordance with the present invention.

-36-

The nucleic acid sequence encoding the first and/or second redox protein may be obtained from separate sources or may be obtained from the same source. In general however, the nucleic acid sequence encoding a redox-fusion polypeptide comprises nucleic acid sequences encoding a first and a second redox protein obtained from the same or a similar biological source. In certain embodiments provided herein, wherein the nucleic acid sequence encoding the first and second redox protein is obtained from the same source, the nucleic acid sequence encoding the first redox protein and second redox protein may be naturally fused. In accordance with a particular embodiment, the nucleic acid sequences encoding the first and second redox protein are preferably obtained from a plant source.

As set forth above, a polypeptide spacer or linker of variable length may separate the first and second redox proteins from each other and/or from the oil-body-targeting-protein; and additional redox proteins (e.g., one or more) may be fused to the first and/or second redox protein.

10

15

The nucleic acid sequences encoding the redox proteins may be altered to improve expression levels for example by optimizing the nucleic acids sequence in accordance with the preferred codon usage for the particular cell type which is selected for expression of the redox proteins, or by altering of motifs known to 20 destabilize mRNAs (see for example: PCT Patent Application 97/02352). Comparison of the codon usage of the redox protein with codon usage of the host will enable the identification of codons that may be changed. For example, typically plant evolution has tended towards a preference for CG rich nucleotide sequences while bacterial evolution has resulted in bias towards AT rich 25 nucleotide sequences. By modifying the nucleic acid sequences to incorporate nucleic acid sequences preferred by the host cell, expression may be optimized. Construction of synthetic genes by altering codon usage is described in for example PCT patent Application 93/07278. The redox proteins may be altered using for example, targeted mutagenesis, random mutagenesis (Shiraishi et al. (1998) Arch. Biochem. Biophys. 358: 104-115; Galkin et al. (1997) Protein Eng. 30 10: 687-690; Carugo et al. (1997) Proteins 28: 10-28; Hurley et al. (1996) Biochemistry 35: 5670-5678) (and/or by the addition of organic solvent

PCT/US01/50240 WO 02/50289

(Holmberg et al. (1999) Protein Eng. 12: 851-856). The polypeptide spacer between the first and second redox protein may be altered in similar ways.

The first and second redox protein may be selected by developing a twodimensional matrix and determining which combination of first and second redox 5 protein is most effective in electron transport using for example, a colorometric reduction assay (Johnson et al (1984) J. of Bact. Vol. 158 3:1061-1069, Luthman et al (1982) Biochemistry Vol 21 26:6628-2233). Combinations of thioredoxin and thioredoxin-reductase may be tested by determining the reduction of wheat storage proteins and milk storage protein beta-lactoglobulin in vitro (Del Val et al. (1999) J. Allerg. Clin. Immunol. 103: 690-697). Using the same strategy polypeptide spacers between the first and second redox proteins may be evaluated for their efficiency.

10

20

30

First and second redox proteins that may be used herein include without limitation any first redox protein and second redox protein selected from the group of redox proteins consisting of cytochromes, such as cytochrome a, cytochrome b and cytochrome c; porphyrin containing proteins, for example hemoglobin; iron-sulfur proteins, such as ferredoxin; flavoproteins such as thioredoxin-reductase, NADH dehydrogenase, succinate dehydrogenase, dihydrolipoyl dehydrogenase, acyl-CoA dehydrogenase, D-amino acid oxidase, xanthine oxidase, orotate reductase and aldehyde oxidase; pyridine-linked dehydrogenases, for example, lactate dehydrogenase, glyceraldehyde-3phosphate dehydrogenase, malate dehydrogenase, and beta-hydroxy-butarate dehydrogenase; and redox active thiol containing proteins such as thioredoxin.

In particular embodiments, the redox proteins provided herein are thioredoxin and its reductant thioredoxin-reductase (which are jointly also referred to herein as "thioredoxin-related" protein(s)). As used herein, the term "thioredoxin" refers to relatively small proteins (typically approximately 12 kDa) that belong to the family of thioltransferases which catalyze oxido-reductions via the formation or hydrolysis of disulfide bonds and are widely, if not universally, distributed throughout the animal plant and bacterial kingdom. The reduces form of thioredoxin is an excellent catalyst for the reduction of even the most intractable disulfide bonds. In order to reduce the oxidized thioredoxin, two

10

15

30

cellular reductants provide the reduction equivalents: reduced ferredoxin and NADPH. These reduction equivalents are supplied to thioredoxin via interaction or association with different thioredoxin-reductases including the NADPH thioredoxin-reductase and ferredoxin thioredoxin-reductase. The supply of these reduction equivalents requires the formation of a heteromultimeric-protein-complex comprising thioredoxin and thioredoxin-reductase. Ferredoxin thioredoxin-reductase is involved in the reduction of plant thioredoxins designated as Trxf and Trxm, both of which are involved in the regulation of photosynthetic processes in the chloroplast. The NADPH/thioredoxin active in plant seeds is designated Trxh (also referred to herein as thioredoxin h-type) and is capable of the reduction of a wide range of proteins thereby functioning as an important cellular redox buffer. Generally, only one kind of thioredoxin, which analogous to the plant Trxh type, is found in bacterial or animal cells. The h-type thioredoxins are capable of being reduced by NADPH and NADPH-thioredoxin reductase.

Exemplary thioredoxins are further characterized as a protein having a core of 5 beta-sheets surrounded by 4 to 6 alpha helixes. Exemplary thioredoxins are further characterized by having an active site containing the consensus amino acid sequence:

20 XCYYCZ,

wherein Y is any amino acid, such as hydrophobic or non-polar amino acids, wherein X can be any of the 20 amino acids, preferably a hydrophobic amino acid, such as a tryptophan, and

Z can be any amino acid, preferably polar amino acids.

In certain embodiments, the thioredoxins for use herein comprise an active site having the amino acid sequence XCGPCZ.

When the cysteines in the active site of thioredoxin or thioredoxin-like proteins are oxidized, they form an intramolecular disulfide bond. In the reduced state, the same active sites are capable of participating in redox reactions through the reversible oxidation of its active site dithiol, to a disulfide and catalyzes dithioldisulfide exchange reactions.

Exemplary thioredoxins are well-known in the art and can be obtained from several organisms including Arabidopsis thaliana (Riveira Madrid et al. (1995) Proc. Natl. Acad. Sci. 92: 5620-5624), wheat (Gautier et al. (1998) Eur. J. Biochem. 252: 314-324); Escherichia coli (Hoeoeg et al (1984) Biosci. Rep. 4; 5 917-923) and thermophylic microorganisms such as Methanococcus jannaschii and Archaeoglobus fulgidus (PCT Patent Application 00/36126). Thioredoxins have also been recombinantly expressed in several host systems including bacteria (Gautier et al. (1998) Eur J. Biochem. 252: 314-324) and plants (PCT Patent Application WO 00/58453) Commercial preparations of E. coli sourced Thioredoxins are readily available from for example: Sigma Cat No. T 0910 Thioredoxin (E. coli, recombinant; expressed in E. coli).

10

Exemplary nucleic acid sequences encoding thioredoxin polypeptides for use herein are readily available from a variety of diverse biological sources including E. coli (Hoeoeg et al. (1984) Biosci. Rep.: 4 917-923); Methanococcus jannaschii and Archaeoglobus fulgidus (PCT Patent Application 00/36126); Arabidopsis thaliana (Rivera-Madrid (1995) Proc. Natl. Acad. Sci. 92: 5620-5624); wheat (Gautier et al (1998) Eur. J. Biochem. 252(2): 314-324); tobacco (Marty et al. (1991) Plant Mol. Biol. 17: 143-148); barley (PCT Patent Application 00/58352); rice (Ishiwatari et al. (1995) Planta 195: 456-463); soybean (Shi et al. (1996) Plant Mol. Biol. 32: 653-662); rapeseed (Bower et al. 20 Plant Cell 8: 1641-1650) and calf (Terashima et al. (1999) DNA Seq. 10(3): 203-205); and the like. In yet other embodiments, exemplary nucleic acids for use herein include those encoding the thioredoxin and thioredoxin-like polypeptide chains set forth as SEQ ID NOs:38, 42, 46 and 50; and those encoding the thioredoxin and thioredoxin-like polypeptide chains set forth in 25 Table 5 as SEQ ID NOs:52-194. The respective nucleic acid sequences encoding the amino acids set forth in SEQ ID NOs:52-194 can be readily identified via the Swiss Protein identifier (accession) numbers provided in Table 5 (in parenthesis).

30 As us d herein, the term "thioredoxin-reductase" refers to a protein that complexes with a flavin, such as FAD. The flavin compound serves as an electron donor for the thioredoxin-reductase protein active site. Thioredoxin

-40-

reductases have a redox active, disulfide bond site capable of reducing thioredoxin. The active site of thioredoxin-reductase contains 2 cysteines. The type of amino acids surrounding the 2 cysteine residues forming the active site can vary as hydrophobic, non-polar or polar. An exemplary thioredoxinreductase is NADPH-thioredoxin-reductase (NTR), which is a cytosolic homodimeric enzyme comprising typically 300-500 amino acids. Crystal structures of both E. coli and plant thioredoxin-reductase have been obtained (Waksman et al. (1994) J. Mol. Biol. 236: 800-816; Dai et al. (1996) J. Mol. Biol. 264:1044-1057). NADPH-thioredoxin-reductases have been expressed in heterologous hosts, for example the Arabidopsis NADPH-thioredoxin-reductase has been expressed in E. coli (Jacquot et al. (1994) J. Mol. Biol. 235; 1357-1363) and wheat (PCT Patent Application 00/58453).

10

25

30

Exemplary nucleic acid sequences encoding thioredoxin-reductase proteins can readily be obtained from a variety of sources, such as from the 15 sequence set forth in Table 5 and the Sequence Listing provide herein, from Arabidopsis (Riveira Madrid et al. (1995) Proc. Natl. Acad. Sci. USA 92: 5620-5624), E. coli (Russel et al. (1988) J. Biol. Chem. 263: 9015-9019); barley (PCT Patent Application 00/58352 and wheat (Gautier et al., (1998) Eur. J. Biochem. 252: 314-324); and the like. In yet other embodiments, exemplary nucleic acids 20 for use herein include those encoding the thioredoxin-reductase polypeptide chains set forth as SEQ ID NOs:8, 9, 10, 40, 44, 48 and 50; and those encoding the thioredoxin-reductase polypeptide chains set forth in Table 5 as SEQ ID NOs:195-313. The respective nucleic acid sequences encoding the amino acids set forth in SEQ ID NOs:195-313 can be readily identified via the Swiss Protein identifier (accession) numbers provided in Table 5 (in parenthesis).

Also contemplated for use in the methods and compositions provided herein are nucleic acid and amino acid homologs that are "substantially homologous" to the thioredoxin and thioredoxin-reductase nucleic and amino acids set forth herein, which includes thioredoxin and thioredoxin-reductase polypeptides encoded by a sequence of nucleotides that hybridizes under conditions of low, moderate or high stringency to the sequence of nucleotides encoding the thioredoxin and thioredoxin-reductase nucleic and amino acids set

forth herein (e.g., in the Examples, Sequence Listing and/or Table 5). As used herein, a DNA or nucleic acid homolog refers to a nucleic acid that includes a preselected conserved nucleotide sequence, such as a sequence encoding a therapeutic polypeptide. By the term "substantially homologous" is meant having at least 80%, preferably at least 90%, most preferably at least 95% homology therewith or a less percentage of homology or identity and conserved biological activity or function.

The terms "homology" and "identity" are often used interchangeably. In this regard, percent homology or identity may be determined, for example, by comparing sequence information using a GAP computer program. The GAP program utilizes the alignment method of Needleman and Wunsch (*J. Mol. Biol.* 48:443 (1970), as revised by Smith and Waterman (*Adv. Appl. Math.* 2:482 (1981). Briefly, the GAP program defines similarity as the number of aligned symbols (i.e., nucleotides or amino acids) which are similar, divided by the total number of symbols in the shorter of the two sequences. The preferred default parameters for the GAP program may include: (1) a unary comparison matrix (containing a value of 1 for identities and 0 for non-identities) and the weighted comparison matrix of Gribskov and Burgess, *Nucl. Acids Res.* 14:6745 (1986), as described by Schwartz and Dayhoff, eds., *ATLAS OF PROTEIN SEQUENCE AND STRUCTURE*, National Biomedical Research Foundation, pp. 353-358 (1979); (2) a penalty of 3.0 for each gap and an additional 0.10 penalty for each symbol in each gap; and (3) no penalty for end gaps.

10

15

20

25

30

By sequence identity, the number of conserved amino acids are determined by standard alignment algorithms programs, and are used with default gap penalties established by each supplier. Substantially homologous nucleic acid molecules would hybridize typically at moderate stringency or at high stringency all along the length of the nucleic acid of interest. Preferably the two molecules will hybridize under conditions of high stringency. Also contemplated are nucleic acid molecules that contain degenerate codons in place of codons in the hybridizing nucleic acid molecule.

Whether any two nucleic acid molecules have nucleotide sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% "identical" can be

30

determined using known computer algorithms such as the "FAST A" program, using for example, the default parameters as in Pearson and Lipman, *Proc. Natl. Acad. Sci. USA 85*:2444 (1988). Alternatively the BLAST function of the National Center for Biotechnology Information database may be used to determine relative sequence identity.

In general, sequences are aligned so that the highest order match is obtained. "Identity" per se has an art-recognized meaning and can be calculated using published techniques. (See, e.g.: Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics 10 and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part I, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). 15 While there exist a number of methods to measure identity between two polynucleotide or polypeptide sequences, the term "identity" is well known to skilled artisans (Carillo, H. & Lipton, D., SIAM J Applied Math 48:1073 (1988)). Methods commonly employed to determine identity or similarity between two sequences include, but are not limited to, those disclosed in Guide to Huge 20 Computers, Martin J. Bishop, ed., Academic Press, San Diego, 1994, and Carillo, H. & Lipton, D., SIAM J Applied Math 48:1073 (1988). Methods to determine identity and similarity are codified in computer programs. Preferred computer program methods to determine identity and similarity between two sequences include, but are not limited to, GCG program package (Devereux, J., et al., Nucleic Acids Research 12(I):387 (1984)), BLASTP, BLASTN, FASTA 25 (Atschul, S.F., et al., J Molec Biol 215:403 (1990)).

Therefore, as used herein, the term "identity" represents a comparison between a test and a reference polypeptide or polynucleotide. For example, a test polypeptide may be defined as any polypeptide that is 90% or more identical to a reference polypeptide.

As used herein, the term at least "90% identical to" refers to percent identities from 90 to 99.99 relative to the reference polypeptides. Identity at a

10

15

20

25

30

level of 90% or more is indicative of the fact that, assuming for exemplification purposes a test and reference polynucleotide length of 100 amino acids are compared. No more than 10% (i.e., 10 out of 100) amino acids in the test polypeptide differs from that of the reference polypeptides. Similar comparisons may be made between a test and reference polynucleotides. Such differences may be represented as point mutations randomly distributed over the entire length of an amino acid sequence or they may be clustered in one or more locations of varying length up to the maximum allowable, e.g. 10/100 amino acid difference (approximately 90% identity). Differences are defined as nucleic acid or amino acid substitutions, or deletions.

As used herein: stringency of hybridization in determining percentage mismatch is as follows:

- 1) high stringency: 0.1 x SSPE, 0.1% SDS, 65°C
- 2) medium stringency: 0.2 x SSPE, 0.1% SDS, 50°C
- 3) low stringency: 1.0 x SSPE, 0.1% SDS, 50°C

Those of skill in this art know that the washing step selects for stable hybrids and also know the ingredients of SSPE (see, e.g., Sambrook, E.F. Fritsch, T. Maniatis, in: Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory Press (1989), vol. 3, p. B.13, see, also, numerous catalogs that describe commonly used laboratory solutions). SSPE is pH 7.4 phosphate-buffered 0.18 NaCl. Further, those of skill in the art recognize that the stability of hybrids is determined by  $T_m$ , which is a function of the sodium ion concentration and temperature ( $T_m = 81.5^{\circ}$  C-16.6( $log_{10}[Na^+]$ ) + 0.41(%G+C)-600/l)), so that the only parameters in the wash conditions critical to hybrid stability are sodium ion concentration in the SSPE (or SSC) and temperature.

It is understood that equivalent stringencies may be achieved using alternative buffers, salts and temperatures. By way of example and not limitation, procedures using conditions of low stringency are as follows (see also Shilo and Weinberg, *Proc. Natl. Acad. Sci. USA*, 78:6789-6792 (1981)): Filters containing DNA are pretreated for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1%

-44-

Ficoll, 1% BSA, and 500  $\mu$ g/ml denatured salmon sperm DNA (10X SSC is 1.5 M sodium chloride, and 0.15 M sodium citrate, adjusted to a pH of 7).

In a particular embodiment, a heteromultimeric-protein-complex is produced as a fusion polypeptide between the first and second redox protein, wherein the first redox protein is thioredoxin and the second redox protein is a thioredoxin-reductase. In one embodiment, the second recombinant polypeptide, e.g., the thioredoxin-reductase is positioned N-terminal relative to the first recombinant polypeptide, e.g., the thioredoxin. Accordingly, any protein which is classified as thioredoxin, such as the thioredoxin component of the NADPH thioredoxin system and the thioredoxin present in the ferredoxin/thioredoxin system also known as TRx and TRm may be used in combination with any thioredoxin-reductase such as the NADPH thioredoxin-reductase and the ferredoxin-thioredoxin-reductase and any other proteins having the capability of reducing thioredoxin. In particular embodiments the thioredoxin and thioredoxin-reductase are plant derived.

In an alternate embodiment, the naturally occurring nucleic acid sequence encoding the thioredoxin/thioredoxin-reductase protein fusion obtainable from *Mycobacterium leprae* (Wieles et al. (1995) J. Biol. Chem. 27:25604-25606) is used, as set forth in the Examples herein.

## 20 Immunoglobulins

10

15

25

30

In another embodiment of the present invention, the multimeric- protein-complexes are immunoglobulins. As used herein "immunoglobulin-polypeptide-chain" refers to a first polypeptide that is capable of associating with a second polypeptide to form an immunologically active (i.e. capable of antigen binding) multimeric-protein-complex. The types of immunoglobulins and immunoglobulin-polypeptide-chains contemplated for use herein include the immunologically active (i.e. antigen binding) portions of a light and heavy chain. Exemplary immunoglobulins and immunoglobulin-polypeptide-chains for use herein include substantially intact immunoglobulins, including any IgG, IgA, IgD, IgE and IgM, as well as any portion of an immunoglobulin, including those portions well-known as Fab fragments, Fab' fragments, F(ab').sub2. fragments and Fv fragments.

WO 02/50289

10

15

30

In this embodiment, the first recombinant polypeptide may be any immunoglobulin heavy chain, including any IgG, IgA, IgD, IgE or IgM heavy chain, and the second recombinant polypeptide may be a kappa or lambda immunoglobulin light chain. Accordingly, provided herein are methods of producing an immunoglobulin, said method comprising: (a) producing in a cell comprising oil bodies, a first immunoglobulin-polypeptide-chain and a second immunoglobulin-polypeptide-chain wherein said first immunoglobulin-polypeptide-chain is capable of associating with said second immunoglobulin-polypeptide-chain to form said immunoglobulin; and (b) associating said immunoglobulin with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said first immunoglobulin-polypeptide-chain.

As set forth herein, the multimeric immunoglobulin is associated with an oil body through an oil-body-targeting-protein. In particular embodiments, the oil-body-targeting-protein may be a fusion polypeptide comprising an oil-body-protein and an immunoglobulin binding protein, such as for example protein A, protein L, and protein G.

In yet another embodiment involving immunoglobulins, the first and second recombinant polypeptides (immunoglobulins) are separately fused to an oil body protein, for example an oleosin or caleosin. For example,

- a) the first recombinant polypeptide may be an immunoglobulin heavy chain, including any IgG, IgA, IgD, IgE or IgM heavy chain, and the second recombinant polypeptide may be a kappa or lambda immunoglobulin light chain; or
  - b) the first recombinant polypeptide may be the variable and first constant domain from an immunoglobulin heavy chain and the second recombinant polypeptide may be a kappa or lambda immunoglobulin light chain; or
  - c) the first recombinant polypeptide may be the variable domain from an immunoglobulin heavy chain and the second recombinant polypeptide may be the variable domain from a kappa or lambda immunoglobulin light chain.

In certain embodiments, the fusion polypeptides are designed or selected to allow the heteromultimeric-protein-complex formation between

-46-

immunoglobulin light and heavy chain sequences on the oil bodies within the cell comprising oil bodies.

Preparation of expression vectors comprising oil-body-targeting-proteins and the first and/or second recombinant polypeptides, multimeric-protein-complexes,

5 heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins.

10

20

25

30

In accordance with the present invention, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and the oil-body-targetingprotein are conveniently produced in a cell. In order to produce the recombinant polypeptides or multimeric-protein-complexes, a nucleic acid sequence encoding either the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and/or the oil-body-targeting-protein are incorporated in a recombinant expression vector. Accordingly, provided herein are recombinant expression vectors comprising the chimeric nucleic acids provided herein suitable for expression of the oil-body-targeting-protein and the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, suitable for the selected cell. The term "suitable for expression in the selected cell" means that the recombinant expression vector contains all nucleic acid sequences required to ensure expression in the selected cell.

Accordingly, the recombinant expression vectors further contain regulatory nucleic acid sequences selected on the basis of the cell which is used

for expression and ensuring initiation and termination of transcription operatively linked to the nucleic acid sequence encoding the recombinant polypeptide or multimeric-protein-complex and/or the oil-body-targeting-protein. Regulatory nucleic acid sequences include promoters, enhancers, silencing elements, 5 ribosome binding sites, Shine-Dalgarno sequences, introns and other expression elements. "Operatively linked" is intended to mean that the nucleic acid sequences comprising the regulatory regions linked to the nucleic acid sequences encoding the recombinant polypeptide or multimeric-protein-complex and/or the oil-body-targeting-protein allow expression in the cell. A typical nucleic acid 10 construct comprises in the 5' to 3' direction a promoter region capable of directing expression, a coding region comprising the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, 15 or the first and/or second thioredoxin-related proteins; and/or an oil-bodytargeting-protein and a termination region functional in the selected cell.

The selection of regulatory sequences will depend on the organism and the cell type in which the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and/or the oil-body-targeting-protein is expressed, and may influence the expression levels of the polypeptide. Regulatory sequences are art-recognized and selected to direct expression of the oil-body-targeting-protein and the recombinant polypeptides or multimeric-protein-complexes in the cell.

20

25

30

Promoters that may be used in bacterial cells include the lac promoter (Blackman et al. (1978) Cell: 13: 65-71), the trp promoter (Masuda et al. (1996) Protein Eng: 9: 101-106) and the T7 promoters (Studier et al. (1986) J. Mol. Biol. 189: 113-130). Promoters functional in plant cells that may be used herein include constitutive promoters such as the 35S CaMV promoter (Rothstein et al. (1987) Gene: 53: 153-161) the actin promoter (McElroy et al. (1990) Plant Cell

2: 163-171) and the ubiquitin promoter (European Patent Application 0 342 926). Other promoters are specific to certain tissues or organs (for example, roots, leaves, flowers or seeds) or cell types (for example, leaf epidermal cells, mesophyll cells or root cortex cells) and or to certain stages of plant development. Timing of expression may be controlled by selecting an inducible promoter, for example the PR-a promoter described in US Patent 5,614,395. Selection of the promoter therefore depends on the desired location and timing of the accumulation of the desired polypeptide. In a particular embodiment, the first and/or second recombinant polypeptides, multimeric-protein-complexes, 10 heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and the oil-body-targeting-protein are expressed in a seed cell and seed specific promoters are utilized. Seed specific promoters that may be used herein include for example the phaseolin promoter (Sengupta-Gopalan et al. (1985) Proc. Natl. Acad. Sci. USA: 82: 3320-3324), and the Arabidopsis 18 kDa oleosin promoter (van Rooijen et al. (1992) Plant. Mol. Biol. 18: 1177-1179). New promoters useful in various plant cell types are constantly discovered. Numerous examples of plant promoters may be found in Ohamuro et al. 20 (Biochem of Pl. (1989) 15: 1-82).

Genetic elements capable of enhancing expression of the polypeptide may be included in the expression vectors. In plant cells these include for example, the untranslated leader sequences from viruses such as the AMV leader sequence (Jobling and Gehrke (1987) Nature: 325: 622-625) and the intron associated with the maize ubiquitin promoter (See: US Patent 5,504,200).

25

30

Transcriptional terminators are generally art recognized and besides serving as a signal for transcription termination serve as a protective element serving to extend the mRNA half-life (Guarneros et al. (1982) Proc. Natl. Acad. Sci. USA: 79: 238-242). In nucleic acid sequences for the expression in plant cells, the transcriptional terminator typically is from about 200 nucleotide to about 1000 nucleotides in length. Terminator sequences that may be used herein include for example, the nopaline synthase termination region (Bevan et

al. (1983) Nucl. Acid. Res.: 11: 369-385), the phaseolin terminator (van der Geest et al. (1994) Plant J.: 6: 413-423), the terminator for the octopine synthase gene of *Agrobacterium tumefaciens* or other similarly functioning elements. Transcriptional terminators can be obtained as described by An (1987) Methods in Enzym. 153: 292). The selection of the transcriptional terminator may have an effect on the rate of transcription.

Accordingly, provided herein are chimeric nucleic acid sequences encoding a first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins. In one embodiment, said nucleic acid comprises:

10

15

20

25

30

- (a) a first nucleic acid sequence encoding an oil-body-targeting-protein operatively linked in reading frame to;
- (b) a second nucleic acid sequence encoding a first recombinant polypeptide, immunoglobulin-polypeptide-chain, or redox protein; linked in reading frame to;
- (c) a third nucleic acid sequence encoding a second recombinant polypeptide, immunoglobulin-polypeptide-chain or redox protein, wherein said first and second recombinant polypeptides, immunoglobulin-polypeptide-chains or redox proteins are capable of forming a multimeric-protein-complex.

In another embodiment, provided herein is an expression vector comprising:

- a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
  - 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked in reading frame to (ii) a nucleic acid sequence encoding a multimeric-fusion-protein, such as a redox fusion polypeptide or immunoglobulin, comprising a first recombinant polypeptide, such as a redox protein or immunoglobulin-polypeptide-chain, linked to a second recombinant polypeptide,

such as a second redox protein or a second immunoglobulin-polypeptide-chain, operatively linked to;

3) a third nucleic acid sequence capable of terminating transcription in said cell.

5

10

20

25

30

The recombinant expression vector further may contain a marker gene. Marker genes that may be used in accordance with the present invention include all genes that allow the distinction of transformed cells from non-transformed cells including all selectable and screenable marker genes. A marker may be a resistance marker such as an antibiotic resistance marker against for example kanamycin, ampicillin, G418, bleomycin hygromycin, chloramphenicol which allows selection of a trait by chemical means or a tolerance marker against for example a chemical agent such as the normally phytotoxic sugar mannose (Negrotto et al. (2000) Plant Cell Rep. 19: 798-803). In plant recombinant expression vectors herbicide resistance markers may conveniently be used for example markers conferring resistance against glyphosate (US Patents 4,940,935 and 5,188,642) or phosphinothricin (White et al. (1990) Nucl. Acids Res. 18: 1062; Spencer et al. (1990) Theor. Appl. Genet. 79: 625-631). Resistance markers to a herbicide when linked in close proximity to the redox protein or oil-body-targeting-protein may be used to maintain selection pressure on a population of plant cells or plants for those plants that have not lost the protein of interest. Screenable markers that may be employed to identify transformants through visual observation include beta-glucuronidase (GUS) (see US Patents US5,268,463 and US5,599,670) and green fluorescent protein (GFP) (Niedz et al. (1995) Plant Cell Rep.: 14: 403).

The recombinant expression vectors further may contain nucleic acid sequences encoding targeting signals ensuring targeting to a cell compartment or organelle. Suitable targeting signals that may be used herein include those that are capable of targeting polypeptides to the endomembrane system. Exemplary targeting signals that may be used herein include targeting signals capable of directing the protein to the periplasm, the cytoplasm, the golgi apparatus, the apoplast (Sijmons et al., 1990, Bio/Technology, 8:217-221) the chloroplast (Comai et al. (1988) J. Biol. Chem. 263: 15104-15109), the mitochondrion, the

peroxisome (Unger et al. (1989) Plant Mol. Biol. 13: 411-418), the ER, the vacuole (Shinshi et al. (1990) Plant Mol. Biol. 14: 357-368 and the oil body. By the inclusion of the appropriate targeting sequences it is possible to direct the oil-body-targeting-protein or the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins, to the desired organelle or cell compartment.

10

20

25

The recombinant expression vectors of the present invention may be prepared in accordance with methodologies well known to those of skill in the art of molecular biology (see for example: Sambrook et al. (1990) Molecular Cloning, 2<sup>nd</sup> ed. Cold Spring Harbor Press). The preparation of these constructs may involve techniques such as restriction digestion, ligation, gel electrophoresis, DNA sequencing and PCR. A wide variety of cloning vectors is available to perform the necessary cloning steps resulting in a recombinant expression vector ensuring expression of the polypeptide. Especially suitable for this purpose are vectors with a replication system that is functional in *Escherichia coli* such as pBR322, the PUC series of vectors, the M13mp series of vectors, pBluescript etc. Typically these vectors contain a marker allowing the selection of transformed cells for example by conferring antibiotic resistance. Nucleic acid sequences may be introduced in these vectors and the vectors may be introduced in *E. coli* grown in an appropriate medium. Vectors may be recovered from cells upon harvesting and lysing the cells.

Recombinant expression vectors suitable for the introduction of nucleic acid sequences in plant cells include *Agrobacterium* and *Rhizobium* based vectors such as the Ti and Ri plasmids. *Agrobacterium* based vectors typically carry at least one T-DNA border sequence and include vectors such pBIN 19 (Bevan (1984) Nucl Acids Res. Vol. 12, 22:8711-8721) and other binary vector systems (for example: US Patent 4,940,838).

30 Production of c lls comprising a first and/or second recombinant polyp ptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, immunoglobulins,

immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein and oil-body-targeting-proteins

In accordance with the present invention, the recombinant expression vectors are introduced into the cell that is selected and the selected cells are 5 grown to produce the first and/or second recombinant polypeptides, multimericprotein-complexes, heteromultimeric-protein-complexes, multimeric-fusionproteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulinpolypeptide-chains, redox-fusion-polypeptides, a first and/or second thioredoxinrelated protein; and the oil-body-targeting-protein either directly or in a progeny cell.

10

20

25

30

Methodologies to introduce recombinant expression vectors into a cell also referred to herein as "transformation" are well known to the art and vary depending on the cell type that is selected. General techniques to transfer the recombinant expression vectors into the cell include electroporation; chemically mediated techniques, for example CaCl2 mediated nucleic acid uptake; particle bombardment (biolistics); the use of naturally infective nucleic acid sequences for example virally derived nucleic acid sequences or when plant cells are used Agrobacterium or Rhizobium derived nucleic acid sequences; PEG mediated nucleic acid uptake, microinjection, and the use of silicone carbide whiskers (Kaeppler et al. (1990) Plant Cell Rep. 9:415-418) all of which may be used herein.

Introduction of the recombinant expression vector into the cell may result in integration of its whole or partial uptake into host cell genome including the chromosomal DNA or the plastid genome. Alternatively the recombinant expression vector may not be integrated into the genome and replicate independently of the host cell's genomic DNA. Genomic integration of the nucleic acid sequence is typically used as it will allow for stable inheritance of the introduced nucleic acid sequences by subsequent generations of cells and the creation of cell, plant or animal lines.

Particular embodiments involve the use of plant cells. Particular plant cells used herein include cells obtainable from Brazil nut (Betholletia excelsa); castor (Riccinus communis); coconut (Cocus nucifera); coriander (Coriandrum

sativum); cotton (Gossypium spp.); groundnut (Arachis hypogaea); jojoba (Simmondsia chinensis); linseed/flax (Linum usitatissimum); maize (Zea mays); mustard (Brassica spp. and Sinapis alba); oil palm (Elaeis guineeis); olive (Olea europaea); rapeseed (Brassica spp.); safflower (Carthamus tinctorius); soybean (Glycine max); squash (Cucurbita maxima); barley (Hordeum vulgare); wheat (Traeticum aestivum) and sunflower (Helianthus annuus).

Transformation methodologies for dicotelydenous plant species are well known. Generally Agrobacterium mediated transformation is utilized because of its high efficiency as well as the general susceptibility by many, if not all dicotelydenous plant species. Agrobacterium transformation generally involves the transfer of a binary vector (e.g. pBIN19) comprising the DNA of interest to an appropriate Agrobacterium strain (e.g. CIB542) by for example tri-parental mating with an E. coli strain carrying the recombinant binary vector and an E. coli strain carrying a helper plasmid capable of mobilization of the binary vector to the target Agrobacterium strain, or by DNA transformation of the Agrobacterium strain (Hofgen et al. Nucl. Acids. Res. (1988) 16: 9877. Other transformation methodologies that may be used to transform dicotelydenous plant species include biolistics (Sanford (1988) Trends in Biotechn. 6: 299-302); electroporation (Fromm et al. (1985) Proc. Natl. Acad. Sci. USA 82: 5824-5828); PEG mediated DNA uptake (Potrykus et al. (1985) Mol. Gen. Genetics 199: 169-177); microinjection (Reich et al. Bio/Techn. (1986) 4: 1001-1004) and silicone carbide whiskers (Kaeppler et al. (1990) Plant Cell Rep. 9: 415-418). The exact transformation methodologies typically vary somewhat depending on the plant species that is used.

10

20

25

30

In a particular embodiment the oil bodies are obtained from safflower and the recombinant proteins are expressed in safflower. Safflower transformation has been described by Baker and Dyer (Plant Cell Rep. (1996) 16: 106-110).

Monocotelydenous plant species may now also be transformed using a variety of methodologies including particle bombardment (Christou et al. (1991) Biotechn. 9: 957-962; Weeks et al. Plant Physiol. (1993) 102: 1077-1084; Gordon-Kamm et al. Plant Cell (1990) 2: 603-618) PEG mediated DNA uptake

(EP 0 292 435; 0 392 225) or *Agrobacterium*-mediated transformation (Goto-Fumiyuki et al (1999) Nature-Biotech. 17 (3):282-286).

Plastid transformation is described in US Patents 5,451,513; 5,545,817 and 5,545,818; and PCT Patent Applications 95/16783; 98/11235 and 00/39313) Basic chloroplast transformation involves the introduction of cloned plastid DNA flanking a selectable marker together with the nucleic acid sequence of interest into a suitable target tissue using for example biolistics or protoplast transformation. Selectable markers that may be used include for example the bacterial aadA gene (Svab et al. (1993) Proc. Natl. Acad. Sci. USA 90: 913-917). Plastid promoters that may be used include for example the tobacco clpP gene promoter (PCT Patent Application 97/06250).

In another embodiment, the invention chimeric nucleic acid constructs provided herein are directly transformed into the plastid genome. Plastid transformation technology is described extensively in U.S. Patent Nos.

15 5,451,513, 5,545,817, 5,545,818 and 5,576,198; in PCT application nos. WO 95/16783 and WO 97/32977; and in McBride et. al., *Proc Natl Acad Sci USA* 91: 7301-7305 (1994), the entire disclosures of all of which are hereby incorporated by reference. In one embodiment, plastid transformation is achieved via biolistics, first carried out in the unicellular green alga

20 *Chlamydomonas reinhardtii* (Boynton *et al.* (1988) *Science* 240:1534-1537)) and then extended to *Nicotiana tabacum* (Svab *et al.* (1990) *Proc Natl Acad Sci USA* 87:8526-8530), combined with selection for cis-acting antibiotic resistance loci (spectinomycin or streptomycin resistance) or complementation of non-photosynthetic mutant phenotypes.

In another embodiment, tobacco plastid transformation is carried out by particle bombardment of leaf or callus tissue, or polyethylene glycol (PEG)-mediated uptake of plasmid DNA by protoplasts, using cloned plastid DNA flanking a selectable antibiotic resistance marker. For example, 1 to 1.5 kb flanking regions, termed targeting sequences, facilitate homologous recombination with the plastid genome and allow the replacement or modification of specific regions of the 156 kb tobacco plastid genome. In one embodiment, point mutations in the plastid 16S rDNA and rps12 genes

25

30

conferring resistance to spectinomycin and/or streptomycin can be utilized as selectable markers for transformation (Svab et al. (1990) Proc Natl Acad Sci USA 87:8526-8530; Staub et al. (1992) Plant Cell 4:39-45, the entire disclosures of which are hereby incorporated by reference), resulting in stable homoplasmic transformants at a frequency of approximately one per 100 bombardments of target leaves. The presence of cloning sites between these markers allows creation of a plastid targeting vector for introduction of foreign genes (Staub et al. (1993) EMBO J 12:601-606, the entire disclosure of which is hereby incorporated by reference). In another embodiment, substantial increases in transformation frequency can be obtained by replacement of the recessive rRNA or r-protein antibiotic resistance genes with a dominant selectable marker, the bacterial aadA gene encoding the spectinomycin-detoxifying enzyme aminoglycoside-3'-adenyltransferase (Svab et al. (1993) Proc Natl Acad Sci USA 90: 913-917, the entire disclosure of which is hereby incorporated by reference). This marker has also been used successfully for high-frequency transformation of the plastid genome of the green alga Chlamydomonas reinhardtii (Goldschmidt-Clermont, M. (1991) Nucl Acids Res 19, 4083-4089, the entire disclosure of which is hereby incorporated by reference). In other embodiments, plastid transformation of protoplasts from tobacco and the moss Physcomitrella can be attained using PEG-mediated DNA uptake (O'Neill et al. (1993) Plant J 20 3:729-738; Koop et al. (1996) Planta 199:193-201, the entire disclosures of which are hereby incorporated by reference).

Both particle bombardment and protoplast transformation are also contemplated for use herein. Plastid transformation of oilseed plants has been successfully carried out in the genera *Arabidopsis* and *Brassica* (Sikdar *et al.* (1998) *Plant Cell Rep* 18:20-24; PCT Application WO 00/39313, the entire disclosures of which are hereby incorporated by reference).

25

30

A chimeric nucleic sequence construct is inserted into a plastid expression cassette including a promoter capable of expressing the construct in plant plastids. A particular promoter capable of expression in a plant plastid is, for example, a promoter isolated from the 5' flanking region upstream of the coding region of a plastid gene, which may come from the same or a different

species, and the native product of which is typically found in a majority of plastid types including those present in non-green tissues. Gene expression in plastids differs from nuclear gene expression and is related to gene expression in prokaryotes (Stern *et al.* (1997) *Trends in Plant Sci* 2:308-315, the entire disclosure of which is hereby incorporated by reference).

10

20

25

30

Plastid promoters generally contain the -35 and -10 elements typical of prokaryotic promoters, and some plastid promoters called PEP (plastid-encoded RNA polymerase) promoters are recognized by an E. coli-like RNA polymerase mostly encoded in the plastid genome, while other plastid promoters called NEP promoters are recognized by a nuclear-encoded RNA polymerase. Both types of plastid promoters are suitable for use herein. Examples of plastid promoters include promoters of clpP genes such as the tobacco clpP gene promoter (WO 97/06250, the entire disclosure of which is hereby incorporated by reference) and the Arabidopsis clpP gene promoter (U.S. Application No. 09/038,878, the entire disclosure of which is hereby incorporated by reference). Another promoter capable of driving expression of a chimeric nucleic acid construct in plant plastids comes from the regulatory region of the plastid 16S ribosomal RNA operon (Harris et al., (1994) Microbiol Rev 58:700-754; Shinozaki et al. (1986) EMBO J 5:2043-2049, the entire disclosures of both of which are hereby incorporated by reference). Other examples of promoters capable of driving expression of a nucleic acid construct in plant plastids include a psbA promoter or am rbcL promoter. A plastid expression cassette preferably further includes a plastid gene 3' untranslated sequence (3' UTR) operatively linked to a chimeric nucleic acid construct of the present invention. The role of untranslated sequences is preferably to direct the 3' processing of the transcribed RNA rather than termination of transcription. An exemplary 3' UTR is a plastid rps16 gene 3' untranslated sequence, or the Arabidopsis plastid psbA gene 3' untranslated sequence. In a further embodiment, a plastid expression cassette includes a poly-G tract instead of a 3' untranslated sequence. A plastid expression cassette also preferably further includes a 5' untranslated sequence (5' UTR) functional in plant plastids, operatively linked to a chimeric nucleic acid construct provided herein.

A plastid expression cassette is contained in a plastid transformation vector, which preferably further includes flanking regions for integration into the plastid genome by homologous recombination. The plastid transformation vector may optionally include at least one plastid origin of replication. The present invention also encompasses a plant plastid transformed with such a plastid transformation vector, wherein the chimeric nucleic acid construct is expressible in the plant plastid. Also encompassed herein is a plant or plant cell, including the progeny thereof, including this plant plastid. In a particular embodiment, the plant or plant cell, including the progeny thereof, is homoplasmic for transgenic plastids.

10

15

20

25

30

Other promoters capable of driving expression of a chimeric nucleic acid construct in plant plastids include transactivator-regulated promoters, preferably heterologous with respect to the plant or to the subcellular organelle or component of the plant cell in which expression is effected. In these cases, the DNA molecule encoding the transactivator is inserted into an appropriate nuclear expression cassette which is transformed into the plant nuclear DNA. The transactivator is targeted to plastids using a plastid transit peptide. The transactivator and the transactivator-driven DNA molecule are brought together either by crossing a selected plastid-transformed line with and a transgenic line containing a DNA molecule encoding the transactivator supplemented with a plastid-targeting sequence and operably linked to a nuclear promoter, or by directly transforming a plastid transformation vector containing the desired DNA molecule into a transgenic line containing a chimeric nucleic acid construct encoding the transactivator supplemented with a plastid-targeting sequence operably linked to a nuclear promoter. If the nuclear promoter is an inducible promoter, in particular a chemically inducible embodiment, expression of the chimeric nucleic acid construct in the plastids of plants is activated by foliar application of a chemical inducer. Such an inducible transactivator-mediated plastid expression system is preferably tightly regulatable, with no detectable expression prior to induction and exceptionally high expression and accumulation of protein following induction.

A particular transactivator is, for example, viral RNA polymerase. Particular promoters of this type are promoters recognized by a single sub-unit RNA polymerase, such as the T7 gene 10 promoter, which is recognized by the bacteriophage T7 DNA-dependent RNA polymerase. The gene encoding the T7 polymerase is preferably transformed into the nuclear genome and the T7 polymerase is targeted to the plastids using a plastid transit peptide. Promoters suitable for nuclear expression of a gene, for example a gene encoding a viral RNA polymerase such as the T7 polymerase, are described above and elsewhere in this application. Expression of chimeric nucleic acid constructs in plastids can be constitutive or can be inducible, and such plastid expression can be also organ- or tissue-specific. Examples of various expression systems are extensively described in WO 98/11235, the entire disclosure of which is hereby incorporated by reference. Thus, in one aspect, the present invention utilizes coupled expression in the nuclear genome of a chloroplast-targeted phage T7 RNA polymerase under the control of the chemically inducible PR-1a promoter, for example of the PR-1 promoter of tobacco, operably linked with a chloroplast reporter transgene regulated by T7 gene 10 promoter/terminator sequences, for example as described in as in US Patent No. 5,614,395 the entire disclosure of which is hereby incorporated by reference. In another embodiment, when plastid transformants homoplasmic for the maternally inherited TR or NTR genes are pollinated by lines expressing the T7 polymerase in the nucleus, F1 plants are obtained that carry both transgene constructs but do not express them until synthesis of large amounts of enzymatically active protein in the plastids is triggered by foliar application of the PR-1a inducer compound benzo(1,2,3)thiadiazole-7-carbothioic acid S-methyl ester (BTH).

10

20

25

30

In a particular embodiment, two or more genes, for example TR and NTR genes, are transcribed from the plastid genome from a single promoter in an operon-like polycistronic gene. In one embodiment, the operon-like polycistronic gene includes an intervening DNA sequence between two genes in the operon-like polycistronic gene. In a particular embodiment, the intervening DNA sequence is not present in the plastid genome to avoid homologous recombination with plastid sequences. In another embodiment, the DNA

sequence is derived from the 5´ untranslated (UTR) region of a non-eukaryotic gene, preferably from a viral 5´UTR, preferably from a 5´UTR derived from a bacterial phage, such as a T7, T3 or SP6 phage. In one embodiment, a portion of the DNA sequence may be modified to prevent the formation of RNA secondary structures in an RNA transcript of the operon-like polycistronic gene, for example between the DNA sequence and the RBS of the downstream gene. Such secondary structures may inhibit or repress the expression of the downstream gene, particularly the initiation of translation. Such RNA secondary structures are predicted by determining their melting temperatures using computer models and programs such a the "mfold" program version 3 (availabl from Zuker and Turner, Washington University School of Medicine, St-Louis, MO) and other methods known to one skilled in the art.

10

15

20

25

30

The presence of the intervening DNA sequence in the operon-like polycistronic gene increases the accessibility of the RBS of the downstream gene, thus resulting in higher rates of expression. Such strategy is applicable to any two or more genes to be transcribed from the plastid genome from a single promoter in an operon-like chimeric heteromultimeric gene.

Following transformation the cells are grown, typically in a selective medium allowing the identification of transformants. Cells may be harvested in accordance with methodologies known to the art. In order to associate the oil bodies with the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and a first and/or second thioredoxin-related protein, the integrity of cells may be disrupted using any physical, chemical or biological methodology capable of disrupting the cells' integrity. These methodologies are generally cell-type dependent and known to the skilled artisan. Where plants are employed they may be regenerated into mature plants using plant tissue culture techniques generally known to the skilled artisan. Seeds may be harvested from mature transformed plants and used to propagate the plant line. Plants may also be crossed and in this manner, contemplated herein is the breeding of cells lines and transgenic plants that vary in genetic

background. It is also possible to cross a plant line comprising the first recombinant polypeptide with a plant line comprising the second recombinant polypeptide. Accordingly, also provided herein are methods of producing in a plant a recombinant multimeric-protein-complex, said method comprising:

- (a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide, such as a redox protein (e.g., a thioredoxin-related protein, and the like) or an immunoglobulin-polypeptide-chain, wherein said first recombinant polypeptide is capable of associating with said oil bodies through an oil-body-targeting-protein;
- (b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide, such as a second redox protein (e.g., a thioredoxin-related protein, and the like) or a second immunoglobulinpolypeptide-chain; and

15

(c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex.

The second recombinant polypeptide may also associate with the oil
bodies. Accordingly, also provided herein are methods of producing in a plant a recombinant multimeric-protein-complex, said method comprising:

(a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide, such as a redox (or thioredoxin-related) protein or immunoglobulin-polypeptide-chain, wherein said first recombinant polypeptide is
capable of associating with said oil bodies through an oil-body-targeting-protein;
(b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide, such as a second redox (thioredoxin-related) protein or a second immunoglobulin-polypeptide-chain, wherein said second recombinant polypeptide is capable of associating with said oil bodies through an oil body targeting protein; and

(c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies

-61-

are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex. Isolation of Oil bodies

The oil bodies provided herein may be obtained from any cell containing oil bodies, including any animal cell; plant cell; fungal cell; for example a yeast cell, algae cell; or bacterial cell. Any process suitable for the isolation oil bodies from cells may be used herein. Processes for the isolation of oil bodies from plant seed cells have been described in US Patents (6,146,645 and 6,183,762) and the isolation of oil bodies from yeast cells has been described by Ting et al. (1997) J. Biol. Chem. 272: 3699-3706).

5

10

15

20

25

30

In certain embodiments, the oil bodies are obtained from a plant cell such as for example a pollen cell; a fruit cell; a spore cell; a nut cell; mesocarp cell; for example the mesocarp cells obtainable from olive (*Olea europaea*) or avocado (*Persea americana*); or a seed cell. In particular embodiments the oil bodies are obtained from a plant seed cell. The seeds can be obtained from a transgenic plant according to the present invention. In particular embodiments, a seed of a transgenic plant according to the present invention contains the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins,

heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or first and/or second thioredoxin-related proteins in a concentration of at least about 0.5% of total cellular seed protein. In further embodiments, a seed of a transgenic plant provided herein contains a recombinant polypeptide or multimeric-protein-complex in a concentration of at least about 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1.0%, 1.25%, 1.5%, 1.75%, 2.0%, 2.25%, 2.5%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10% or more, of total cellular seed protein. The upper limits of the recombinant polypeptide or multimeric-protein-complex concentration can be up to about 8%, 9%, 10%,

11%, 12%, 13%, 14%, 15%. Thus, the ranges at least about 0.5% up to about 15%; at least about 1.0% up to about 10%; and at least about 5% up to about 8% are among the various ranges contemplated herein.

Among the plant seeds useful in this regard are plant seeds obtainable from the group of plant species consisting of Brazil nut (Betholletia excelsa); castor (Riccinus communis); coconut (Cocus nucifera); coriander (Coriandrum sativum); cotton (Gossypium spp.); groundnut (Arachis hypogaea); jojoba (Simmondsia chinensis); linseed/flax (Linum usitatissimum); maize (Zea mays); mustard (Brassica spp. and Sinapis alba); oil palm (Elaeis guineeis); olive (Olea europaea); rapeseed (Brassica spp.); safflower (Carthamus tinctorius); soybean (Glycine max); squash (Cucurbita maxima); sunflower (Helianthus annuus); barley (Hordeum vulgare); wheat (Traeticum aestivum) and mixtures thereof. In a particular embodiment, oil bodies are obtainable from the seeds obtainable from safflower (Carthamus tinctorius).

In order to prepare oil bodies from plant seeds, plants are grown and allowed to set seed in accordance with common agricultural practices. Thus, the present invention also provides seeds comprising oil bodies, wherein said oil bodies further comprise invention multimeric-protein-complexes described herein. Upon harvesting the seed and, if necessary the removal of large insoluble materials such as stones or seed hulls, by for example sieving or rinsing, any process suitable for the isolation of oil bodies from seeds may be used herein. A typical process involves grinding of the seeds followed by an aqueous extraction process.

15

20

25

30

Seed grinding may be accomplished by any comminuting process resulting in a substantial disruption of the seed cell membrane and cell walls without compromising the structural integrity of the oil bodies present in the seed cell. Suitable grinding processes in this regard include mechanical pressing and milling of the seed. Wet milling processes such as described for cotton (Lawhon et al. (1977) J. Am. Oil Chem. Soc. 63: 533-534) and soybean (US Patent 3,971,856; Carter et al. (1974) J. Am. Oil Chem. Soc. 51: 137-141) are particularly useful in this regard. Suitable milling equipment capable of industrial scale seed milling include colloid mills, disc mills, pin mills, orbital mills, IKA mills and industrial scale homogenizers. The selection of the milling equipment will depend on the seed, which is selected, as well as the throughput requirement.

Solid contaminants such as seed hulls, fibrous materials, undissolved carbohydrates, proteins and other insoluble contaminants are subsequently preferably removed from the ground seed fraction using size exclusion based methodologies such as filtering or gravitational based methods such as a centrifugation based separation process. Centrifugation may be accomplished using for example a decantation centrifuge such as a HASCO 200 2-phase decantation centrifuge or an NX310B (Alpha Laval). Operating conditions are selected such that a substantial portion of the insoluble contaminants and sediments and may be separated from the soluble fraction.

Following the removal of insolubles the oil body fraction may be separated from the aqueous fraction. Gravitational based methods as well as size exclusion based technologies may be used. Gravitational based methods that may be used include centrifugation using for example a tubular bowl centrifuge such as a Sharples AS-16 or AS-46 (Alpha Laval), a disc stack centrifuge or a hydrocyclone, or separation of the phases under natural gravitation. Size exclusion methodologies that may be used include membrane ultra filtration and crossflow microfiltration.

10

15

20

30

Separation of solids and separation of the oil body phase from the aqueous phase may also be carried out concomitantly using gravity based separation methods or size exclusion based methods.

The oil body preparations obtained at this stage in the process are generally relatively crude and depending on the application of the oil bodies, it may be desirable to remove additional contaminants. Any process capable of removing additional seed contaminants may be used in this regard. Conveniently the removal of these contaminants from the oil body preparation may be accomplished by resuspending the oil body preparation in an aqueous phase and re-centrifuging the resuspended fraction, a process referred to herein as "washing the oil bodies". The washing conditions selected may vary depending on the desired purity of the oil body fractions. For example where oil bodies are used in pharmaceutical compositions, generally a higher degree of purity may be desirable than when the oil bodies are used in food preparations. The oil bodies may be washed one or more times depending on the desired purity and the ionic

strength, pH and temperature may all be varied. Analytical techniques may be used to monitor the removal of contaminants. For example SDS gel electrophoresis may be employed to monitor the removal of seed proteins.

The entire oil body isolation process may be performed in a batch wise fashion or continuous flow. In a particular embodiment, industrial scale continuous flow processes are utilized.

5

10

Through the application of these and similar techniques the skilled artisan is able to obtain oil bodies from any cell comprising oil bodies. The skilled artisan will recognize that generally the process will vary somewhat depending on the cell type that is selected. However, such variations may be made without departing from the scope and spirit of the present invention.

Association of the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, the first and/or second thioredoxin-related proteins with oil bodies.

In accordance with the present invention, the oil bodies are associated with either the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, 20 heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, the first and/or second thioredoxin-related proteins through association with an oil-body-targeting-protein capable of association with these multimeric-protein-complexes and the oil bodies. As used herein the phrase "associating the oil bodies with the multimeric-protein-25 complex" means that the oil bodies are brought in proximity of the multimericprotein-complexes in a manner that allows the association of the oil bodies with either the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-30 chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins. The association of the oil bodies with the multimeric-proteincomplexes is accomplished by association of the oil-body-targeting-protein with

both the oil body and with the multimeric-protein-complex. In particular embodiments, the cells expressing the multimeric-protein-complex associate with the oil bodies that are obtainable from these same cells, which permits the convenient production and isolation of the multimeric-protein-complex, including the first and/or second recombinant polypeptides, heteromultimeric-proteincomplexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, in an oil body-comprising host cell system. Accordingly, in one embodiment, the association of the oil body with the multimeric-protein-complex is accomplished intracellularly during the growth of the cell. For example, a redox fusion polypeptide may be fused to an oil-body-protein and the chimeric protein may be expressed in oil bodycontaining plant seeds. Isolation of the oil bodies from the seeds in this case results in isolation of oil bodies comprising either the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins. In another embodiment, in which the multimeric-protein-complex associates with oil bodies obtainable from the same cells in which the complex is produced, the association of the oil bodies with the multimeric-protein-complex is accomplished upon disrupting the cell's integrity.

10

15

20

25

30

For example, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins may be expressed in such a manner that it is targeted to the endomembrane system of the seed cells. Oil bodies present in the same seed cells comprising an oil-body-targeting-protein capable of association with these multimeric-protein-complexes, for example an oleosin linked to a single chain antibody capable of association with a recombinant polypeptide or multimeric-protein-complex, may then associate with the

-66-

recombinant polypeptide or multimeric-protein-complex upon grinding of the seed.

In accordance with this embodiment, plant seed cells comprising a light and heavy chain of an immunoglobulin targeted to the plant apoplast can be prepared. These particular seed cells are prepared to further comprise oil bodies associated with an oil-body-targeting-protein capable of association with the immunoglobulin, such as for example, an oleosin-protein A fusion protein, and the like. Upon grinding of the seed, the oil bodies comprising protein A associate with the immunoglobulin through binding.

10

15

20

25

30

In yet another embodiment, the oil bodies used to associate with the multimeric-protein-complex are obtained from a cellular source different from the cell comprising the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, such as from a separate plant line. For example, oil bodies associated with protein A may be prepared from one plant line. These oil bodies may then be mixed with ground seeds comprising an apoplastically expressed light and heavy chain constituting an immunoglobulin. Alternatively, a plant line comprising oil bodies associated with protein A may be crossed with a plant line comprising an immunoglobulin.

The first recombinant polypeptide, second recombinant polypeptide and oil-body-targeting-protein may also be prepared in separate cellular compartments. Association of the first polypeptide, second polypeptide, and oil body then may occur upon disruption of the cell's integrity. For example, various mechanisms for targeting gene products are known to exist in plants, and the sequences controlling the functioning of these mechanisms have been characterized in some detail. For example, the targeting of gene products to the chloroplast is controlled by a transit sequence found at the amino terminal end of various proteins which is cleaved during chloroplast import to yield the mature protein (Comai *et al.* (1988) *J Biol Chem* 263: 15104-15109). Other gene products are localized to other organelles such as the mitochondrion and the

peroxisome (Unger et al. (1989) Plant Mol Biol 13:411-418). The cDNAs encoding these products can be manipulated to target heterologous gene products to these organelles. In addition, sequences have been characterized which cause the targeting of gene products to other cell compartments.

Amino terminal sequences are responsible for targeting to the ER, the apoplast, and extracellular secretion from aleurone cells (Koehler & Ho (1990) *Plant Cell* 2:769-783). Additionally, amino terminal sequences in conjunction with carboxy terminal sequences are responsible for vacuolar targeting of gene products (Shinshi *et al.*, (1990) *Plant Mol Biol* 14:357-368). By the fusion of the appropriate targeting sequences described above to transgene sequences of interest it is possible to direct the transgene product to the desired organelle or cell compartment.

As hereinbefore mentioned, the redox protein obtained using the methods provided herein is enzymatically active while associated with the oil body. Preferably the redox protein is at least 5 times more active when produced as a redox fusion polypeptide with a second redox protein relative to its production in association with an oil body as a non-fusion polypeptide (i.e. without the second redox protein). More preferably the redox protein is at least 10 times more

The activity of the redox fusion polypeptide may be determined in accordance with methodologies generally known to the art (see for example: Johnson et al (1984) J. of Bact. Vol. 158 3:1061-1069) and may be optimized by for example the addition of detergents, including ionic and non-ionic detergents.

active when produced as a redox fusion polypeptide.

## 25 Formulation of Oil Bodies

5

In accordance with a particular embodiment, the oil bodies comprising the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, are preferably formulated into an emulsion. The emulsion is preferably used in the preparation of a pharmaceutical composition, personal care or a food

product. In emulsified form, the oil body offers certain desirable properties, such as for example excellent compatibility with the human skin.

It particular embodiments, the oil body formulation is stabilized so that a final product may be obtained which may be stored and preserved for longer periods of time. As used herein, the term "stabilized oil body preparation" refers to an oil body preparation that is prepared so that the formulation does not undergo undesirable physical or chemical alterations when the oil body preparation is stored. The stabilization requirements may vary depending on the final product. For example personal care products are preferably stable for at least one year at room temperature while additionally being able to withstand short temperature fluctuations. Pharmaceutical formulations may in some cases be less stable as they may be stored at lower temperatures thereby preventing the occurrence of undesirable reactions.

In general, stabilization techniques that may be used herein include any and all methods for the preservation of biological material including the addition of chemical agents, temperature modulation based methodologies, radiation-based technologies and combinations thereof. In particular embodiments small amounts of stabilizing chemical agents are mixed with the oil body formulation to achieve stabilization. These chemical agents include *inter alia* preservatives, antioxidants, acids, salts, bases, viscosity modifying agents, emulsifiers, gelling agents and mixtures thereof and may all be used to stabilize the oil body preparation. In view of the presence of the redox fusion polypeptide the stabilizing agent is generally selected to be compatible with and resulting in good enzymatic function of the redox fusion polypeptide.

20

25

30

Diagnostic parameters to assess the stability of the oil body preparation may be as desired and include all parameters indicative of undesirable qualitative or quantitative changes with respect to chemical or physical stability. Typical parameters to assess the oil body preparation over time include color, odor, viscosity, texture, pH and microbial growth, and enzymatic activity.

In particular embodiments, the oil body formulation is stabilized prior to the addition of further ingredients that may be used to prepare the final product. Howevera, in other embodiments, it is nevertheless possible to formulate the

final formulation using non-stabilized oil bodies and stabilize the final formulation.

The final preparations may be obtained using one or more additional ingredients and any formulation process suitable for the preparation of a formulation comprising oil bodies. Ingredients and processes employed will generally vary depending on the desired use of the final product, will be art recognized and may be as desired. Ingredients and processes that may be used herein include those described in US Patents (US Patents 6,146,645 and 6,183,762) which are incorporated by reference herein.

In particular embodiments, the redox fusion polypeptide comprises a thioredoxin and a thioredoxin-reductase. Accordingly, provided herein are oil bodies comprising a thioredoxin/thioredoxin-reductase fusion polypeptide. Also provided herein is a formulation containing oil bodies comprising a thioredoxin/thioredoxin-reductase fusion capable of treating or protecting a target against oxidative stress. The stress of the target is treated or prevented by contacting the target with the formulation. The target may be any substance susceptible to oxidative stress, including any molecule, molecular complex, cell, tissue or organ.

10

15

30

In another embodiment, provided herein is a formulation containing oil bodies comprising a thioredoxin/thioredoxin-reductase fusion capable of chemically reducing a target. Contacting the target with the formulation reduces the target. The target may be any substance susceptible to reduction, including any molecule or molecular complex. Particularly susceptible targets in this regard are the disulfide bonds present in proteins.

The oil bodies comprising thioredoxin/thioredoxin-reductase may be used to prepare formulations used to reduce the allergenicity of food or increase the digestibility of food. Preferably, the method of reducing the food allergenicity is practiced by mixing the thioredoxin/thioredoxin-reductase comprising oil bodies with food or food ingredients selected from a variety of sources including for example wheat flour, wheat dough, milk, cheese, soya, yogurt and ice cream. The thioredoxin/thioredoxin-reductase comprising oil bodies may also be used to increase the digestibility of milk as well as other disulfide containing proteins (Jiao, J. et al. (1992) J. Agric. Food Chem 40: 2333-2336). Further food

applications include the use of the oil thioredoxin/thioredoxin-reductase comprising oil bodies as a food additive to enhance dough strength and bread quality properties (Wong et al., (1993) J. Cereal Chem. 70: 113-114; Kobrehel et al. (1994) Gluten Proteins: Association of Cereal Research; Detmold, Germany).

5

25

30

Also provided herein are pharmaceutical compositions comprising, in a pharmaceutically active carrier: oil bodies comprising a thioredoxin/thioredoxinreductase; oil bodies comprising multimeric-protein-complexes, such as heteromultimeric-protein-complexes; isolated thioredoxin/thioredoxin-reductase 10 fusion proteins; or isolated multimeric-protein-complexes. These pharmaceutical compositions may be used for the treatment of reperfusion injury (Aota et al. (1996) J. Cardiov. Pharmacol. (1996) 27: 727-732), cataracts (US Patent US 4,771,036), chronic obstructive pulmonary disease (COPD) (MacNee et al. (1999) Am. J. Respir. Crit. Care Med. 160:S58-S65), diabetes (Hotta et al. J. Exp. Med. 188: 1445-1451), envenomation (PCT Patent Application 99/20122; US Patent 5,792,506), bronchiopulmonary disease (MacNee (2000) Chest 117:3035-3175); malignancies (PCT Patent Application 91/04320) and the alleviation of the allergenic potential of airborne, for example pollen- derived, and contact allergens (PCT Patent Application 00/44781). Other diseases or 20 conditions that may be treated with the pharmaceutical compositions provided herein include: psoriasis, wound healing, sepsis, Gl bleeding, intestinal bowel disease (IBD), ulcers, transplantation, GERD (gastro esophageal reflux disease).

In another embodiment, the pharmaceutical compositions provided herein, particularly those comprising one or more redox proteins alone or in combination with oil bodies, can be used in the treatment of inflammatory and viral diseases by reductively inactivating phospholipase A2, one of the contributing factors in inflammatory diseases. Additionally, the redox fusion polypeptide system has been found to function as a self-defense mechanism in response to environmental stimuli, including oxidative stress caused by UV-generated free radicals. Consequently, redox proteins, e.g., oleosin-thioredoxin, oleosin-thioredoxin-reductase, the various redox fusion polypeptides described herein, provide beneficial effects in certain skin conditions such as psoriasis, skin

-71-

cancer, dandruff, diaper rash, dermatitis, acne, sun damage, aging, inflammation, and the like.

10

15

20

25

30

In another embodiment, oil-body-thioredoxin-related fusion proteins, e.g., oleosin-Thioredoxin-reductase, can also be used as a venom antidote. Many animal venoms and other toxins contain disulfide bonds, including all snake venom neurotoxins, some bacterial neurotoxins including tetanus and botulinum A, bee venom phospholipase A<sub>2</sub>, and scorpion venom. In a further embodiment, the redox protein related pharmaceutical compositions provided herein can be used to inactivate venom toxins by reduction of disulfide bonds. A method of treating an individual suffering from the effects of a venom or toxin can include the step of administering an effective dose of a pharmaceutical composition, in a pharmaceutically effective carrier in an amount sufficient to relieve or reverse the effects of the venom toxin on the individual.

The pharmaceutical compositions provided herein are preferably formulated for single dosage administration. The concentrations of the compounds in the formulations are effective for delivery of an amount, upon administration, that is effective for the intended treatment. Typically, the compositions are formulated for single dosage administration. To formulate a composition, the weight fraction of a compound or mixture thereof is dissolved, suspended, dispersed or otherwise mixed in a selected vehicle at an effective concentration such that the treated condition is relieved or ameliorated. Pharmaceutical carriers or vehicles suitable for administration of the compounds provided herein include any such carriers known to those skilled in the art to be suitable for the particular mode of administration.

In addition, the compounds may be formulated as the sole pharmaceutically active ingredient in the composition or may be combined with other active ingredients. Liposomal suspensions, including tissue-targeted liposomes, may also be suitable as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled in the art. For example, liposome formulations may be prepared as described in U.S. Patent No. 4,522,811.

The active compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the patient treated. The therapeutically effective concentration may be determined empirically by testing the compounds in known in vitro and in vivo systems, such as the assays provided herein.

The concentration of active compound in the drug composition will depend on absorption, inactivation and excretion rates of the active compound, the physicochemical characteristics of the compound, the dosage schedule, and amount administered as well as other factors known to those of skill in the art.

10

15

20

25

30

Typically a therapeutically effective dosage is contemplated. The amounts administered may be on the order of 0.001 to 1 mg/ml, preferably about 0.005-0.05 mg/ml, more preferably about 0.01 mg/ml, of blood volume. Pharmaceutical dosage unit forms are prepared to provide from about 1 mg to about 1000 mg and preferably from about 10 to about 500 mg, more preferably about 25-75 mg of the essential active ingredient or a combination of essential ingredients per dosage unit form. The precise dosage can be empirically determined.

The active ingredient may be administered at once, or may be divided into a number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment is a function of the disease being treated and may be determined empirically using known testing protocols or by extrapolation from in vivo or in vitro test data. It is to be noted that concentrations and dosage values may also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or use of the claimed compositions and combinations containing them.

Preferred pharmaceutically acceptable derivatives include acids, salts, esters, hydrates, solvates and prodrug forms. The derivative is typically selected

such that its pharmacokinetic properties are superior to the corresponding neutral compound.

Thus, effective concentrations or amounts of one or more of the compounds provided herein or pharmaceutically acceptable derivatives thereof are mixed with a suitable pharmaceutical carrier or vehicle for systemic, topical or local administration to form pharmaceutical compositions. Compounds are included in an amount effective for ameliorating or treating the disorder for which treatment is contemplated. The concentration of active compound in the composition will depend on absorption, inactivation, excretion rates of the active compound, the dosage schedule, amount administered, particular formulation as well as other factors known to those of skill in the art.

10

20

25

30

Solutions or suspensions used for parenteral, intradermal, subcutaneous, or topical application can include any of the following components: a sterile diluent, such as water for injection, saline solution, fixed oil, polyethylene glycol, glycerine, propylene glycol or other synthetic solvent; antimicrobial agents, such as benzyl alcohol and methyl parabens; antioxidants, such as ascorbic acid and sodium bisulfite; chelating agents, such as ethylenediaminetetraacetic acid (EDTA); buffers, such as acetates, citrates and phosphates; and agents for the adjustment of tonicity such as sodium chloride or dextrose. Parenteral preparations can be enclosed in ampules, disposable syringes or single or multiple dose vials made of glass, plastic or other suitable material.

In instances in which the compounds exhibit insufficient solubility, methods for solubilizing compounds may be used. Such methods are known to those of skill in this art, and include, but are not limited to, using cosolvents, such as dimethylsulfoxide (DMSO), using surfactants, such as Tween<sup>®</sup>, or dissolution in aqueous sodium bicarbonate. Derivatives of the compounds, such as prodrugs of the compounds may also be used in formulating effective pharmaceutical compositions. For ophthalmic indications, the compositions are formulated in an ophthalmically acceptable carrier. For the ophthalmic uses herein, local administration, either by topical administration or by injection is preferred. Time release formulations are also desirable. Typically, the

compositions are formulated for single dosage administration, so that a single dose administers an effective amount.

Upon mixing or addition of the compound with the vehicle, the resulting mixture may be a solution, suspension, emulsion or other composition. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. If necessary, pharmaceutically acceptable salts or other derivatives of the compounds are prepared.

The compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the patient treated. It is understood that number and degree of side effects depends upon the condition for which the compounds are administered. For example, certain toxic and undesirable side effects are tolerated when treating life-threatening illnesses that would not be tolerated when treating disorders of lesser consequence.

10

15

The compounds can also be mixed with other active materials, that do not impair the desired action, or with materials that supplement the desired action known to those of skill in the art. The formulations of the compounds and agents for use herein include those suitable for oral, rectal, topical, 20 inhalational, buccal (e.g., sublingual), parenteral (e.g., subcutaneous, intramuscular, intradermal, or intravenous), transdermal administration or any route. The most suitable route in any given case will depend on the nature and severity of the condition being treated and on the nature of the particular active compound which is being used. The formulations are provided for administration to humans and animals in unit dosage forms, such as tablets, capsules, pills, 25 powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil-water emulsions containing suitable quantities of the compounds or pharmaceutically acceptable derivatives thereof. The pharmaceutically therapeutically active compounds and derivatives thereof are typically formulated and administered in unit-dosage forms or multiple-dosage forms. Unit-dose forms as used herein refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art.

-75-

Each unit-dose contains a predetermined quantity of the therapeutically active compound sufficient to produce the desired therapeutic effect, in association with the required pharmaceutically acceptable carrier, vehicle or diluent. Examples of unit-dose forms include ampoules and syringes and individually packaged tablets or capsules. Unit-dose forms may be administered in fractions or multiples thereof. A multiple-dose form is a plurality of identical unit-dosage forms packaged in a single container to be administered in segregated unit-dose form. Examples of multiple-dose forms include vials, bottles of tablets or capsules or bottles of pints or gallons. Hence, multiple dose form is a multiple of unit-doses which are not segregated in packaging.

10

15

20

The composition can contain along with the active ingredient: a diluent such as lactose, sucrose, dicalcium phosphate, or carboxymethylcellulose; a lubricant, such as magnesium stearate, calcium stearate and talc; and a binder such as starch, natural gums, such as gum acaciagelatin, glucose, molasses, polivinylpyrrolidine, celluloses and derivatives thereof, povidone, crospovidones and other such binders known to those of skill in the art. Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, or otherwise mixing an active compound as defined above and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, glycols, ethanol, and the like, to thereby form a solution or suspension. If desired, the pharmaceutical composition to be administered may also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, or solubilizing agents, pH buffering agents and the like, for example, acetate, sodium citrate, cyclodextrine 25 derivatives, sorbitan monolaurate, triethanolamine sodium acetate, triethanolamine oleate, and other such agents. Methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art (see, e.g., Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pa., 15th Edition, 1975). The composition or formulation to be administered will contain a quantity of the active compound in an amount sufficient to alleviate the symptoms of the treated subject.

Dosage forms or compositions containing active ingredient in the range of 0.005% to 100% with the balance made up from non-toxic carrier may be prepared. For oral administration, the pharmaceutical compositions may take the form of, for example, tablets or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (e.g., pregelatinized maize starch, polyvinyl pyrrolidone or hydroxypropyl methylcellulose); fillers (e.g., lactose, microcrystalline cellulose or calcium hydrogen phosphate); lubricants (e.g., magnesium stearate, talc or silica); disintegrants (e.g., potato starch or sodium starch glycolate); or wetting agents (e.g., sodium lauryl sulphate). The tablets may be coated by methods well-known in the art.

10

20

25

30

The pharmaceutical preparation may also be in liquid form, for example, solutions, syrups or suspensions, or may be presented as a drug product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (e.g., sorbitol syrup, cellulose derivatives or hydrogenated edible fats); emulsifying agents (e.g., lecithin or acacia); non-aqueous vehicles (e.g., almond oil, oily esters, or fractionated vegetable oils); and preservatives (e.g., methyl or propyl-p-hydroxybenzoates or sorbic acid).

Formulations suitable for rectal administration are preferably presented as unit dose suppositories. These may be prepared by admixing the active compound with one or more conventional solid carriers, for example, cocoa butter, and then shaping the resulting mixture.

Formulations suitable for topical application to the skin or to the eye preferably take the form of an ointment, cream, lotion, paste, gel, spray, aerosol and oil. Carriers which may be used include vaseline, lanoline, polyethylene glycols, alcohols, and combinations of two or more thereof. The topical formulations may further advantageously contain 0.05 to 15 percent by weight of thickeners selected from among hydroxypropyl methyl cellulose, methyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, poly (alkylene glycols), poly/hydroxyalkyl, (meth)acrylates or poly(meth)acrylamides. A topical

formulation is often applied by instillation or as an ointment into the conjunctival sac. It can also be used for irrigation or lubrication of the eye, facial sinuses, and external auditory meatus. It may also be injected into the anterior eye chamber and other places. The topical formulations in the liquid state may be also present in a hydrophilic three-dimensional polymer matrix in the form of a strip, contact lens, and the like from which the active components are released.

For administration by inhalation, the compounds for use herein can be delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol, the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, e.g., gelatin, for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

Formulations suitable for buccal (sublingual) administration include, for example, lozenges containing the active compound in a flavored base, usually sucrose and acacia or tragacanth; and pastilles containing the compound in an inert base such as gelatin and glycerin or sucrose and acacia.

15

20

25

30

The compounds may be formulated for parenteral administration by injection, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampules or in multi-dose containers, with an added preservative. The compositions may be suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in powder form for reconstitution with a suitable vehicle, e.g., sterile pyrogen-free water or other solvents, before use.

Formulations suitable for transdermal administration may be presented as discrete patches adapted to remain in intimate contact with the epidermis of the recipient for a prolonged period of time. Such patches suitably contain the active compound as an optionally buffered aqueous solution of, for example, 0.1 to 0.2 M concentration with respect to the active compound. Formulations

suitable for transdermal administration may also be delivered by iontophoresis (see, e.g., Pharmaceutical Research 3 (6), 318 (1986)) and typically take the form of an optionally buffered aqueous solution of the active compound.

The pharmaceutical compositions may also be administered by controlled release means and/or delivery devices (see, e.g., in U.S. Patent Nos. 3,536,809; 3,598,123; 3,630,200; 3,845,770; 3,847,770; 3,916,899; 4,008,719; 4,687,610; 4,769,027; 5,059,595; 5,073,543; 5,120,548; 5,354,566; 5,591,767; 5,639,476; 5,674,533 and 5,733,566).

Desirable blood levels may be maintained by a continuous infusion of the active agent as ascertained by plasma levels. It should be noted that the attending physician would know how to and when to terminate, interrupt or adjust therapy to lower dosage due to toxicity, or bone marrow, liver or kidney dysfunctions. Conversely, the attending physician would also know how to and when to adjust treatment to higher levels if the clinical response is not adequate (precluding toxic side effects).

10

15

20

25

30

The efficacy and/or toxicity of the pharmaceutical compositions provided herein, alone or in combination with other agents can also be assessed by the methods known in the art (See generally, O'Reilly, *Investigational New Drugs*, 15:5-13 (1997)).

The active compounds or pharmaceutically acceptable derivatives may be prepared with carriers that protect the compound against rapid elimination from the body, such as time release formulations or coatings.

Kits containing the compositions and/or the combinations with instructions for administration thereof are provided. The kit may further include a needle or syringe, preferably packaged in sterile form, for injecting the complex, and/or a packaged alcohol pad. Instructions are optionally included for administration of the active agent by a clinician or by the patient.

Finally, the pharmaceutical compositions provided herein containing any of the preceding agents may be packaged as articles of manufacture containing packaging material, a compound or suitable derivative thereof provided herein, which is effective for treatment of a diseases or disorders contemplated herein, within the packaging material, and a label that indicates that the compound or a

suitable derivative thereof is for treating the diseases or disorders contemplated herein. The label can optionally include the disorders for which the therapy is warranted.

Also provided herein are personal care formulations containing oil bodies comprising a thioredoxin/thioredoxin-reductase fusion polypeptide. Personal care products comprising thioredoxin and thioredoxin-reductase are disclosed in for example Japanese Patent Applications JP9012471A2, JP103743A2, and JP1129785A2 Personal care formulations that may be prepared in accordance with the present invention include formulations capable of improving the physical appearance of skin exposed to detrimental environmental stimuli resulting in oxidative stress for example oxidative stress caused by UV-generated free-radicals. The oil bodies comprising thioredoxin/thioredoxin-reductase may also be used to prepare hair care products as described in US Patent Nos. 4,935,231 and 4,973,475 (incorporated herein by reference in their entirety).

The following examples are included for illustrative purposes only and are not intended to limit the scope of the invention.

### **EXAMPLE 1**

## Isolation of thioredoxin and NADPH thioredoxin-reductase genes

10

15

25

30

An Arabidopsis silique cDNA library CD4-12 was obtained from the

Arabidopsis Biological Resource Centre (ABRC, http://aims.cps.msu.edu)

Arabidopsis stock centre and used as a template for the isolation of the thioredoxin h (Trxh) and thioredoxin-reductase genes from Arabidopsis. For the isolation of the Trxh gene the following primers were synthesized:

GVR833: 5' TACCATGGCTTCGGAAGAAGGA 3' (SEQ ID NO:1)

The sequence identical to the 5' end of the Trxh gene as published in Rivera-Madrid et al, (1993) Plant Physiol 102: 327-328, is indicated in bold. Underlined is an Ncol restriction site to facilitate cloning. GVR834: 5' GAAAGCTTAAGCCAAGTGTTTG 3' (SEQ ID NO:2)

The sequence complementary to the 3' end of the Trxh gene as published in Rivera-Madrid et al, (1993) Plant Physiol 102: 327-328, is indicated in bold. Underlined is an HindIII restriction site to facilitate cloning.

-80-

A Polymerase Chain Reaction (PCR) was carried out using GVR833 and GVR834 as primers and the cDNA library CD4-12 as a template. The resulted PCR fragment was isolated, cloned into pBluescript and sequenced. The isolated sequence encoding Trxh was identical to the published Trxh gene sequence (Rivera-Madrid et al, (1993) Plant Physiol 102: 327-328). The pBluescript vector containing the Trxh gene is called pSBS2500.

For the isolation of the thioredoxin-reductase gene the following primers were synthesized:

GVR836: 5' GGCCAGCACACTACCATGAATGGTCTCGAAACTCAC 3' (SEQ ID NO:3). The sequence identical to the 5' end of the thioredoxin-reductase gene as published (Jacquot et al, J Mol Biol. (1994) 235 (4):1357-63), is indicated in bold).

GVR837: 5' TTAAGCTTCAATCACTCTTACCTTGCTG 3' (SEQ ID NO:4).

A Polymerase Chain Reaction (PCR) was carried out using GVR836 and GVR837 as primers and the cDNA library CD4-12 as a template. The resulted PCR fragment was isolated, cloned into pBluescript and sequenced. The pBluescript vector containing the thioredoxin-reductase gene is called pSBS2502.

A total of three clones were sequenced, the sequence of each of the three clones were identical to each other. However, as depicted in Figure 1 this sequence indicated several nucleotide differences compared to the published thioredoxin-reductase gene sequence published (Jacquot et al, J Mol Biol. (1994) 235 (4):1357-63.). The complete coding sequence and its deduced amino acid sequence is shown in SEQ ID NO:10. As a result of the nucleotide differences between the published sequence and the sequence isolated in Example 1, several amino acid changes are also predicted. A comparison of the deduced amino acid sequence of the published NADPH thioredoxin-reductase sequence thioredoxin-reductase (ATTHIREDB, Jacquot et al, J Mol Biol. (1994) 235 (4):1357-63.) with the sequence isolated in Example 1 (TR) is shown in Figure 3.

20

25

-81-

### **EXAMPLE 2**

## Construction of plant expression vectors.

20

25

Expression vectors were constructed to allow for the seed specific overexpression of thioredoxin and NADPH thioredoxin-reductase in seeds. Vectors 5 were constructed to allow for over-expression in its natural subcellular location and for accumulation on oil bodies.

## Construction of plant transformation vector pSBS2520.

The Arabidopsis thioredoxin h gene as described in example 1 was placed under the regulatory control of the phaseolin promoter and the phaseolin terminator derived from the common bean Phaseolus vulgaris (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan et al., (1985) PNAS USA 82: 3320-3324)). A gene splicing by overlap extension technique (Horton et al. (1989) 15: 61-68) was used to fuse the phaseolin promoter to the Trxh gene. Standard molecular biology laboratory techniques (see eg: Sambrook et al. (1990) Molecular Cloning, 2<sup>nd</sup> ed. Cold Spring Harbor Press) were used to furnish 15 the phaseolin promoter and terminator with Pst I and HindIII/KpnI sites respectively (see SEQ ID NO:14). Standard molecular biology laboratory techniques were also used to place the phaseolin terminator downstream from the Trxh gene. The Pstl-phaseolin promoter- Trxh-phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-Kpnl sites of pSBS3000 (pSBS3000 is a derivative from the Agrobacterium binary plasmid pPZP221 (Hajdukiewicz et al., 1994, Plant Molec. Biol. 25: 989-994). In pSBS3000, the CaMV35S promoter-gentamycin resistance gene-CAMV 35S terminator of pPZP221 was replaced with parsley ubiquitin promoter-phosphinothricin acetyl transferase gene-parsley ubiquitin termination sequence to confer resistance to the herbicide glufosinate ammonium.) The resulting plasmid is called pSBS2520. The sequence of the phaseolin promoter-Arabidopsis Trxh-phaseolin terminator sequence is shown in SEQ ID NO:14.

## Construction of plant transformation vector pSBS2510.

30 The 3' coding sequence of an Arabidopsis oleosin gene (van Rooijen et al (1992) Plant Mol. Biol. 18: 1177-1179) was altered to contain an Ncol site. The Ncol-HindIII fragment from v ctor pSBS2500 (Example 1) containing the Trxh was

ligated to the coding sequence of this Arabidopsis oleosin utilizing this Ncol restriction site. A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan et al., 5 (1985) PNAS USA 82: 3320-3324) containing a synthetic Pstl site (see construction of pSBS2520) to the coding sequence of the Arabidopsis oleosin. Standard molecular biology laboratory techniques (see eg: Sambrook et al. (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were again used to clone the HindIII KpnI fragment containing the phaseolin terminator (see construction of pSBS2520) downstream of the Trxh gene. The Pstl-phaseolin promoter- oleosin- Trxh-phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-Kpnl sites of pSBS3000. The resulting plasmid is called pSBS2510. The sequence of the phaseolin promoter-oleosin Trxh-phaseolin terminator sequence is shown in SEQ ID NO:16.

## Construction of plant transformation vector pSBS2521.

10

15

20

25

30

This vector contains the same genetic elements as the insert of pSBS2510 except the Trxh gene is fused to the 5' end of the oleosin gene. The 3' oleosin coding sequence including its native stopcodon (van Rooijen et al (1992) Plant Mol. Biol. 18: 1177-1179) was furnished with a Hindll cloning site. Again a gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter to the Trxh gene and to fuse the Trxh gene to the oleosin sequence. Standard molecular biology laboratory techniques (see eg: Sambrook et al. (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were again used to clone the Hindlll KpnI fragment containing the phaseolin terminator (see construction of pSBS2520) downstream of the oleosin gene. The Pstl-phaseolin promoter- Trxh oleosin- phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-Kpnl sites of pSBS3000. The resulting plasmid is called pSBS2521. The sequence of the phaseolin promoter- Trxh oleosin -phaseolin terminator sequence is shown in SEQ ID NO:19.

## Construction of plant transformation vector pSBS2527.

The Arabidopsis NADPH thioredoxin-reductase gene as described in example 1 was placed under the regulatory control of the phaseolin promoter and the

phaseolin terminator derived from the common bean *Phaseolus vulgaris* (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan *et al.*, (1985) PNAS USA 82: 3320-3324). A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter to the thioredoxin-reductase gene. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2<sup>nd</sup> ed. Cold Spring Harbor Press) were used to furnish the phaseolin promoter and terminator with Pstl and Hindlll/Kpnl sites respectively (see SEQ ID NO:14). Standard molecular biology laboratory techniques were also used to place the phaseolin terminator downstream from the thioredoxin-reductase gene. The Pstl-phaseolin promoter-thioredoxin-reductase-phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-Kpnl sites of pSBS3000 The resulting plasmid is called pSBS2527. The sequence of the phaseolin promoter-*Arabidopsis* thioredoxin-reductase-phaseolin terminator sequence is shown in SEQ ID NO:22.

### Construction of plant transformation vector pSBS2531.

10

15

20

25

A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan *et al.*, (1985) PNAS USA 82: 3320-3324) to the coding sequence of the *Arabidopsis* oleosin. The same gene splicing technique was used to fuse the oleosin gene to the thioredoxin-reductase coding sequence. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2<sup>nd</sup> ed. Cold Spring Harbor Press) were again used to clone the Hindlll Kpnl fragment containing the phaseolin downstream of the thioredoxin-reductase gene. The Pstl-phaseolin promoter- oleosin- thioredoxin-reductase -phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-Kpnl sites of pSBS3000. The resulting plasmid is called pSBS2531. The sequence of the phaseolin promoter-oleosin thioredoxin-reductase -phaseolin terminator sequence is shown in SEQ ID NO:24.

## Construction of plant transformation vector pSBS2529

30 This vector contains the same genetic elements as the insert of pSBS2531 except the thioredoxin-reductase gene is fused to the 5' end of the oleosin gene. The 3' oleosin coding sequence including its native stopcodon (van Rooijen et al.

-84-

(1992) Plant Mol. Biol.18: 1177-1179) was furnished with a HindIII cloning site. Again a gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter to the thioredoxin-reductase gene and to fuse the thioredoxin-reductase gene to the oleosin sequence. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2<sup>nd</sup> ed. Cold Spring Harbor Press) were again used to clone the HindIII KpnI fragment containing the phaseolin terminator (see construction of pSBS2520) downstream of the oleosin gene. The PstI-phaseolin promoter- thioredoxin-reductase oleosin- phaseolin terminator-KpnI insert sequence was cloned into the PstI-KpnI sites of pSBS3000. The resulting plasmid is called pSBS2529. The sequence of the phaseolin promoter-thioredoxin-reductase oleosin -phaseolin terminator sequence is shown in SEQ ID

## Construction of plant transformation vector pSBS2530.

10

NO:27.

15 A plant transformation was constructed containing the Mycobacterium Legrae thioredoxin-reductase /thioredoxin gene (Mlep TR/Trxh). A construct called pHIS/TR/Trxh (Wieles et al (1995) J Biol Chem 270:25604-25606) was obtained from the department of Immunohematology and Blood bank, Leiden University, The Netherlands and use as a template for PCR to generate pSBS2530. The 20 construction of pSBS2530 was identical to the construction of pSBS2531 except that the Mlep TR/Trxh gene was used instead of the Arabidopsis thioredoxin-reductase gene. A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan et al., (1985) PNAS USA 82: 3320-3324) to the coding sequence of the Arabidopsis oleosin. The same gene splicing technique was used to fuse the oleosin gene to the Mlep TR/Trxh coding sequence. Standard molecular biology laboratory techniques (see eg: Sambrook et al. (1990) Molecular Cloning, 2<sup>rd</sup> ed. Cold Spring Harbor Press) were again used to clone the Hindlll-KpnI fragment 30 containing the phaseolin downstream of the Mlep TR/Trxh gene. The Pstlphaseolin promoter- oleosin- Mlep TR/Trxh -phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-KpnI sites of pSBS3000. The resulting

RECTIFIED SHEET (RULE 91)

plasmid is called pSBS2530. The sequence of the phaseolin promoter-oleosin *Mlep* TR/Trxh -phaseolin terminator sequence is shown in SEQ ID NO:30.

## Construction of plant transformation vector pSBS2542.

From initial activity assays (Figure 4), it was apparent that oil bodies expressing the oleosin-*M. lep* TR/Trxh fusion protein contained considerable reducing activity. It was anticipated that a similar oleosin fusion construct encoding the *Arabidopsis* thioredoxin-reductase and thioredoxin proteins would behave in an analogous manner. Molecular modeling was used to aid in the design of such a construct. Primers were designed (thioredoxin link-L: 5'-

10 ACTGGAGATGTTGACTCGACGGATACTACGGATTGGTCGACGG
CTATGGAAGAAGGACAAGTGATCGCCTGC-3'; (SEQ ID NO:5), and thioredoxin link-R:

5'-ATCCGTCGAGTCAACATCTCCAGTTTCCTCGGTGGTCTCGTTAGCCTTCGAT CCAGCAATCTCTTGTAAGAATGCTCTGC-3'; (SEQ ID NO:6) to code for a synthetic linker peptide between the thioredoxin-reductase and thioredoxin proteins. These primers were used in conjunction with primers GVR 873 (5'-GTGGAAGCT TATGGAGATGGAG-3'; SEQ ID NO:7) and GVR834 (5'-GAAAGCTTAAGCCAAGTGTTTG-3'; SEQ ID NO:2) to amplify a region coding for a thioredoxin-reductase-linker region-thioredoxin utilizing a gene splicing by overlap extension technique (Horton et al (1989) 15:61-68). The thioredoxin-reductase-linker-thioredoxin encoding sequence was then cloned into a pre-existing pSBS3000 vector using standard molecular biology techniques (Sambrook et al (1990) Molecular Cloning 2<sup>nd</sup> Edition Cold Spring Harbour Press). The resulting plasmid was called pSBS2542. The sequence of the phaseolin

20

25

30

promoter-oleosin-thioredoxin-reductase-linker-thioredoxin-phaseolin terminator region is shown in SEQ ID NO:33. An amino acid sequence comparison between this *Arabidopsis* thioredoxin-reductase-linker-thioredoxin and the *M. leprae* TR/Trxh protein is shown in Figure 12.

Plasmids pSBS2510, pSBS2520, pSBS2521, pSBS2527, pSBS2529, pSBS2530, pSBS2531 and pSBS2542 were electroporated into *Agrobacterium* strain EHA101. These *Agrobacterium* strains were used to transform *Arabidopsis*. *Arabidopsis* transformation was done essentially as described in

"Arabidopsis Protocols; Methods in molecular biology Vol 82. Edited by Martinez-Zapater JM and Salinas J. ISBN 0-89603-391-0 pg 259-266 (1998) except the putative transgenic plants were selected on agarose plates containing 80µM L-phosphinothricine, after they were transplanted to soil and allowed to set seed.

## **EXAMPLE 3**

<u>Polyacrylamide gelelectrophoresis and immunoblotting of transgenic seed</u> <u>extracts.</u>

10 Source of Arabidopsis thioredoxin, thioredoxin-reductase and oleosin antibodies.

The Arabidopsis thioredoxin and thioredoxin-reductase genes were cloned in frame in bacterial expression vector pRSETB (Invitrogen) to allow for the overexpression of Arabidopsis thioredoxin and thioredoxin-reductase proteins.

These proteins were purified using standard protocols (see eg Invitrogen protocol) and used to raise antibodies in rabbits using standard biochemical techniques (See eg Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989). The *Arabidopsis* oleosin gene genes was cloned in frame in bacterial expression vector pRSETB (Invitrogen) to allow for the overexpression
Arabidopsis oleosin protein. This protein was purified using standard protocols (see eg Invitrogen protocol) and used to prepare mouse monoclonal antibodies using standard biochemical techniques (See eg Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989).

Preparation of total Arabidopsis seed extracts for PAGE. Arabidopsis

seeds were ground in approximately 20 volumes of 2% SDS, 50 mM Tris-Cl,,
this extract was boiled, spun and the supernatant was prepared for
polyacrylamide gelelectrophoresis (PAGE) using standard protocols.

Preparation of Arabidopsis oil-body-protein extracts.

Arabidopsis seeds were ground in approximately 20 volumes of water and spun in a microfuge. The oil bodies were recovered and washed sequentially with approximately 20 volumes of water, a high stringency wash buffer, containing 8M urea and 100 mM sodiumcarbonate and water. After this last wash the

30

oil bodies are prepared for poly acrylamide gelelectrophoresis (PAGE) using standard protocols.

# Analysis of seed and oil body extracts from plants transformed with pSB\$2510

5 Total seed and oil body protein extracts from plants transformed with pSBS2510 were loaded onto polyacrylamide gels and either stained with coomassie brilliant blue or electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against Arabidopsis thioredoxin, or a monoclonal antibody raised against the Arabidopsis 18.5 kDa oleosin and visualized using alkaline phosphatase. Expression of the oleosin-10 thioredoxin results in an additional band of 31.2 kDa. The results indicate that the thioredoxin antibodies are immunologically reactive with a band of the right predicted molecular weight (31.2 kDa), and the oleosin antibodies are also immunologically reactive with a band of the right predicted molecular weight for the fusion protein (31.2 kDa) in addition to a band corresponding to the native Arabidopsis oleosin (18.5 kDa). This indicates that oleosin-thioredoxin is expressed in Arabidopsis seeds and is correctly targeted to oil bodies.

# Analysis of seed and oil body extracts from plants transformed with p\$B\$2521

Total seed and oil body protein extracts from plants transformed with 20 pSBS25121 were loaded onto polyacrylamide gels and either stained with Coomassie brilliant blue or electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against Arabidopsis thioredoxin, or a monoclonal antibody raised against the Arabidopsis 18.5 kDa oleosin and visualized using alkaline phosphatase. Expression of the thioredoxin-oleosin results in an additional band of 31.2 kDa. The results indicate that the thioredoxin antibodies are immunologically reactive with a band of the right predicted molecular weight (31.2 kDa), and the oleosin antibodies are also immunologically reactive with a band of the right predicted molecular weight for the fusion protein (31.2 kDa) in addition to a band corresponding to the native Arabidopsis oleosin (18.5 kDa). This indicates that thioredoxinoleosin is expressed in Arabidopsis seeds and is correctly targeted to oil bodies.

25

30

**RECTIFIED SHEET (RULE 91)** 

-88-

Analysis of seed extracts from plants transformed with pSBS2520 Total seed extracts from plants transformed with pSBS2520 were loaded onto polyacrylamide gels and either stained with Coomassie brilliant blue or electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against Arabidopsis thioredoxin and visualized using alkaline phosphatase. The results indicated that the thioredoxin antibodies are immunologically reactive with a band of approximately the right predicted molecular weight (12 kDa). Untransformed seeds do not show a detectable thioredoxin band.

# Analysis of seed and oil body extracts from plants transformed with pSBS2529

10

20

25

Total seed and oilbody protein extracts from plants transformed with pSBS2529 were loaded onto polyacrylamide gels and electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against *Arabidopsis* thioredoxin-reductase, or a monoclonal antibody raised against the *Arabidopsis* 18.5 kDa oleosin and visualized using alkaline phosphatase. Expression of the thioredoxin-reductase -oleosin results in an additional band of 53.8 kDa. The results indicate that the thioredoxin-reductase antibodies are immunologically reactive with a band of the right predicted molecular weight for the fusion protein (53.8 kDa), the oleosin antibodies are also immunologically reactive with a band of the right predicted molecular weight (53.8 kDa) in addition to a band corresponding to the native *Arabidopsis* oleosin (18.5 kDa). This indicates that thioredoxin-reductase-oleosin is expressed in *Arabidopsis* seeds.

Analysis of seed extracts from plants transformed with pSBS2527 Total seed extracts from plants transformed with pSBS2527 were loaded onto polyacrylamide gels and electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against Arabidopsis thioredoxin-reductase and visualized using alkaline phosphatase. The thioredoxin-reductase antibodies are immunologically reactive with a band of approximately the right predicted molecular weight for the (35.3 kDa). Untransformed seeds do not show a detectable thioredoxin band.

-89-

Analysis of seed extracts from plants transformed with pSBS2531 A protein gel and immunoblot was prepared assaying the expression of oleosin-DMSR in Arabidopsis T2 seeds and correct targeting to Arabidopsis oil bodies. The expected molecular weight based on the deduced amino acid sequence is 5 calculated to be 53,817 Da. In the oil body extract of the transgenic oleosinthioredoxin-reductase sample an extra band of approximately 54 kDa was observed. This band was confirmed to be oleosin-thioredoxin-reductase by immunoblotting. From the polyacrylamide gel it was observed that the expression of the oleosin -Thioredoxin-reductase is about double compared to the expression of the major 18.5 kDa Arabidopsis oleosin. This represents approximately 2-4 % of total seed protein.

Analysis of seed extracts from plants transformed with pSBS2530 A protein gel and immunoblot was prepared assaying the expression of oleosin-M.lep TR/Trxh in Arabidopsis T2 seeds and the correct targeting to Arabidopsis 15 oil bodies. The expected molecular weight based on the deduced amino acid sequence is calculated to be 67,550 Da. In the oil body extract of the transgenic oleosin-M.lep TR/Trxh sample an extra band of approximately 68 kDa was observed. This band was confirmed to be oleosin-M.lep TR/Trxh by immunoblotting. From the polyacrylamide gel it was observed that the expression of the oleosin-M.lep TR/Trxh is similar to the expression of the major 18.5 kDa Arabidopsis oleosin. This represents approximately 1-2 % of total seed protein.

20

30

Analysis of seed extracts from plants transformed with pSBS2542 Crude oil body extracts from pSBS2542 lines were prepared by grinding 100µg of seed in 1 mL of 100mM Tris buffer at pH 7.5. The samples were then centrifuged in order to isolate the oil body fraction. The oil body fraction was then loaded on an SDS polyacrylamide gel for expression analysis. A Coomassie stained gel revealed that the synthetic fusion accumulated to high levels in crude oil body extracts from 3 of the 4 lines tested. It was estimated that the fusion protein represented approximately 2-5% of total seed protein. Furthermore, western blots utilizing either anti-thioredoxin or anti-thioredoxin-reductase antibodies

-90-

confirmed that the over expressed 70 kDa protein was indeed oleosinthioredoxin-reductase-linker-thioredoxin.

# **EXAMPLE 4**

Biological activity of thioredoxin and thioredoxin-reductase transformants Initial reduction assays:

## DTNB assay

25

30

The activity of the thioredoxin and thioredoxin reductase was determined using a colorimetric DTNB [5,5'-dithiolbis (2-nitrobenzoic acid)] assay. The

10 assay was performed in a 700 μL reaction volume containing 100mM Tris-Cl pH 8.0, 5 mM EDTA, 200μM DTNB [5,5'-dithiolbis (2-nitrobenzoic acid)] and 200μM NADPH. If thioredoxin-reductase and thioredoxin are added, NADPH will reduce the thioredoxin-reductase, which will then reduce thioredoxin, which will, in turn, reduce DTNB (see equations below).

- NADPH<sub>2</sub> + thioredoxin-reductase<sub>ox</sub> ----> thioredoxin-reductase<sub>red</sub> + NADP<sup>+</sup> thioredoxin-reductase<sub>red</sub> + thioredoxin<sub>ox</sub> -----> thioredoxin<sub>red</sub> + thioredoxin-reductase<sub>ox</sub> thioredoxin<sub>red</sub> + DTNB<sub>ox</sub> ------> 2(2-nitro-5-mercaptobenzoic acid) + thioredoxin<sub>ox</sub>
- The formation of the yellow product was monitored by measuring the OD<sub>412</sub> in a spectrophotometer after a set period of time (usually 0.5-2 hours). The results of initial activity assays are shown in the bar graph in Figure 4 and described below.

Initially, 100 µg of total seed proteins were added from each of the *Arabidopsis* transgenic lines, pSBS2520 (cytosolic thioredoxin) and pSBS2527 (cytosolic thioredoxin-reductase), which corresponds to approximately 1 µg of cytosolic thioredoxin and thioredoxin-reductase used in the assay. In this case, the amount of DTNB reduced was comparable to the reduction caused by 1 µg each of *E. coli* thioredoxin and thioredoxin-reductase. In these plant seed samples, background readings were very low when only one of the 2 extracts (either cytosolic thioredoxin or cytosolic thioredoxin-reductase; Figure 4, bars 3 and 6, respectively) was added to the reaction, along with wild type oil bodies.

-91-

Analysis with oil body fractions from transgenic seeds revealed that *Arabidopsis* thioredoxin and thioredoxin-reductase were substantially less active when fused to oleosins on oil bodies. Approximately 300 μg of crude, unwashed oil-body-protein was used in the assay (which corresponds to 10-30μg of thioredoxin-oleosin (pSBS 2521; Figure 4, bar 2), oleosin-thioredoxin (pSBS 2510, Figure 4, bar 1), thioredoxin-reductase-oleosin (pSBS 2529, Figure 4, bar 5), or oleosin-thioredoxin-reductase (pSBS 2531, Figure 4, bar 4). The oil-body-proteins were tested in conjunction with 100μg of total seed protein containing approximately 1μg of cytosolic thioredoxin (pSBS 2520) or thioredoxin-reductase (pSBS 2527).

In such assays, pSBS2529 (thioredoxin-reductase-oleosin) and pSBS2531 (oleosin-thioredoxin-reductase) do contain reductase activity when combined with cytosolic thioredoxin from pSBS2520 (see Figure 4, bars 7 and 8, respectively). Experiments estimated that the reductase activity of oleosin-thioredoxin-reductase was about 10-15% that of the cytosolic thioredoxin-reductase. The addition of tween at a final concentration of 0.4% could enhance this activity 2 or 3 fold. Interestingly, oleosin-thioredoxin-reductase (pSBS 2531) appears to be capable of reducing DTNB in the absence of added thioredoxin, although added thioredoxin causes significantly more DTNB reduction (see Figure 4; compare bar 4 W.T. + oleosin-thioredoxin-reductase to bar 7 thioredoxin + oleosin-thioredoxin-reductase). Experiments with pSBS2521 (thioredoxin-oleosin) or pSBS2510 (oleosin-thioredoxin) combined with cytosolic thioredoxin-reductase from pSBS2527 (see Figure 4, bars 10 and 11, respectively) indicate that thioredoxin activity of these fusions is undetectable at these concentrations.

15

20

25

30

Oil bodies from the transgenic *Arabidopsis* line, pSBS2530 (oleosin-*M.lep* TR/Trxh) contain significant thioredoxin/thioredoxin-reductase activity (see Figure 4, bar 12). One hundred micrograms of crude oil body protein for pSBS2530 was tested (corresponding to approximately 5µg of oleosin- *M.lep* TR/trxh fusion) in the assay. Based on the assay, it was estimated that this fusion is about 25-40% as active as cytosolic *Arabidopsis* thioredoxin and thioredoxin-reductase (Figure 4, bar 9) when comparing specific activity.

-92-

# Insulin reduction assay

10

20

25

30

The results from the DTNB assays were confirmed with insulin reduction assays. This assay contained insulin at a final concentration of 1mg/mL in  $100\text{mM KH}_2\text{PO}_4$  pH 7.0 + 5 mM EDTA. In the presence of NADPH ( $500\mu\text{M}$ ), thioredoxin, and thioredoxin-reductase, insulin is reduced and precipitates from the solution. Normally, insulin reduction is followed by measuring turbidity at OD 650. Alternatively, one can measure the conversion of NADPH<sub>2</sub> to NADP+ by monitoring the decrease in absorbance at 340 nm.

Both of the assays are difficult to measure when oil bodies are present, due to interference with the spectrophotometer readings. However, qualitative data could be obtained by centrifuging the tubes after a set period of time, and determining if an insulin pellet was present (oil bodies float to the top, while the insulin precipitate pellets out). Alternatively, samples could be filtered after a set period of time, and the change in absorbance at 340 nm could be measured. As mentioned previously, the results of the insulin reduction assays agreed with those of the DTNB assay, with the exception of the observation that pSBS2531 (oleosin-thioredoxin-reductase) only reduced insulin in the presence of free thioredoxin from pSBS2520.

Assays on seeds from Arabidopsis crosses that co-express oleosinthioredoxin and oleosin-thioredoxin-reductase.

Based upon initial DTNB and insulin reduction assays, it was apparent that mixing oil bodies from oleosin<->thioredoxin and oleosin<->thioredoxin-reductase transgenic seeds resulted in very limited reducing activity (Note: the <-> indicates both configurations of oleosin fusions; ie. oleosin<->thioredoxin would represent oleosin-thioredoxin and thioredoxin-oleosin fusions).

To determine whether having oleosin <-> thioredoxin and oleosin <-> thioredoxin-reductase proteins present on the same oil body would have a positive effect on the reducing activity of these proteins, crosses were set up to generate double transgenic *Arabidopsis* lines. The crosses are illustrated in Table 2.

-93-

TABLE 2

|     | Male                           |   | · Female                   | Confirmed double transgenic lines (PCR and Western Blot) |
|-----|--------------------------------|---|----------------------------|--|
|     | oleo-thioredoxin               | х | oleo-thioredoxin-reductase | 4  |
| 5   | oleo-thioredoxin               | х | thioredoxin-reductase-oleo | 1  |
|     | thioredoxin-oleo               | X | oleo-thioredoxin-reductase | 0  |
|     | thioredoxin-oleo               | X | thioredoxin-reductase-oleo | 4  |
|     | oleo-thioredoxin-<br>reductase | X | oleo-thioredoxin           | 2  |
| 10  | oleo-thioredoxin-<br>reductase | X | thioredoxin-oleo           | 0  |
| •   | thioredoxin-<br>reductase-oleo | Х | oleo-thioredoxin           | 7  |
| 15. | thioredoxin-<br>reductase-oleo | X | thioredoxin-oleo           | 0  |

20

30

Seeds from Arabidopsis crosses were germinated on PPT plates and the seedlings were transferred to soil after approximately 2 weeks. PCR experiments on DNA isolated from the seedlings identified a number of plants which contain both an oleosin <-> thioredoxin and an oleosin <-> thioredoxinreductase gene construct within their genome.

Seeds were harvested from these plants for expression and activity assays. Western blots were carried out to confirm expression of both oleosin <->thioredoxin and oleosin<->thioredoxin-reductase in the lines. DTNB and 25 insulin reduction assays were also performed to compare activity between single transgenic parent lines and the double transgenic offspring and results are summarized in Table 3. Table 3 summarizes DTNB reducing activity of various transgenic lines. The last 2 rows compare mixing oil bodies from single transgenic parent lines to using oil bodies from double transgenic offspring. Relative activity for the E. coli thioredoxin and thioredoxin mixture is set at 100 percent.

-94-

TABLE 3

| Source Material  | Relative Activity (%) |
|--|-----------------------|
| E.coli trx + NTR   | 100                   |
| Arabidopsis "free" thioredoxin +<br>thioredoxin-reductase<br>(pSBS2520 + pSBS2527)                         | 100                   |
| oleosin- <i>M. lep</i> TR/Trxh<br>(pSBS2530)   | ~30                   |
| Oleosin<->thioredoxin-reductase + oleosin<->thioredoxin (mixing oil bodies from single-transgenic parents) | ~3                    |
| Oleosin<->thioredoxin-reductase X<br>oleosin<->thioredoxin<br>(various double transgenic lines)            | ~50                   |

15

20

10

5

Based on DTNB and insulin reduction assays, it is evident that double transgenic plants co-expressing oleosin<->thioredoxin and oleosin<->thioredoxin-reductase on the same, single oil body contained significantly more reducing activity compared to mixing oil bodies from single transgenic oleosin<->thioredoxin and oleosin<->thioredoxin-reductase lines. It was additionally apparent that oil body extracts from co-expressing lines contained more reducing activity compared to line pSBS2530 (oleosin-*M. lep* TR/Trxh), which was previously identified as the line containing the highest reducing activity from oil bodies.

25

These results suggest that the creation of double transgenic lines (either through crossing or by co-transforming 2 expression constructs into plants) may represent one means by which we could solve our initial problem of not being able to generate reducing activity by mixing oil bodies from oleosin<->thioredoxin and oleosin<->thioredoxin-reductase single transgenic lines.

30

Assays on seeds from Arabidopsis pSBS2542 transgenic lines that express oleosin-thioredoxin-reductase-linker-thioredoxin.

Oil body extracts from four pSBS2542 lines were tested for reducing activity in DTNB and insulin reduction assays, using standard protocols described previously. Again, oil body extracts containing the oleosin-thioredoxin-

reductase-linker-thioredoxin protein possessed significant reducing activity. Based on such assays, it was revealed that the oleosin-thioredoxin-reductase-linker-thioredoxin synthetic fusion protein was more active than the oleosin-*M. lep* TR/Trxh fusion. Furthermore, oil bodies containing the oleosin-thioredoxin-reductase-linker-thioredoxin protein appeared to have more reducing activity compared to oil bodies from double transgenic lines that co-expressed oleosin<->thioredoxin and oleosin<->thioredoxin-reductase. The results comparing reducing activity for the various thioredoxin-reductase/thioredoxin constructs is summarized in Table 4. Table 4 summarizes DTNB reducing activity of various transgenic lines. The pSBS2542 line expressing oleosin-thioredoxin-reductase-linker-thioredoxin contains significant reducing activity, comparable to the "free" forms of *Arabidopsis* thioredoxin and thioredoxin-reductase and the equivalent *E. coli* proteins. Relative activity for the *E. coli* thioredoxin and thioredoxin mixture is set at 100 percent.

15

10

**TABLE 4** 

| Source Material  | Relative Activity (%) |
|--|-----------------------|
| E.coli trx + NTR   | 100                   |
| Arabidopsis "free" thioredoxin + thioredoxin-<br>reductase<br>(pSBS2520 + pSBS2527)                        | 100                   |
| oleosin- <i>M. lep</i> TR/Trxh<br>(pSBS2530)   | ~30                   |
| Oleosin<->thioredoxin-reductase + oleosin<->thioredoxin (mixing oil bodies from single-transgenic parents) | ~3                    |
| Oleosin<->thioredoxin-reductase X oleosin<->thioredoxin (various double transgenic lines)                  | <sub>,</sub> ~50      |
| Oleosin-thioredoxin-reductase-linker-thioredoxin (pSBS2542)  | ~75-100               |

25

20

30

Reduction assays comparing the utilization of NADH vs. NADPH as a cofactor (electron donor) for the thioredoxin-reductase/thioredoxin system.

DTNB and insulin reduction assays were conducted as described previously, except that NADH was substituted for NADPH as an electron donor in the system utilizing *E. coli* thioredoxin-reductase and thioredoxin. Thus, a comparison was conducted of the utilization of NADH versus NADPH as a cofactor for the *E. coli* thioredoxin-reductase/ thioredoxin system. For the DTNB assay, the reaction mixture consisted of 400 μM DTNB, 10 μg/mL *E. coli* thioredoxin, and 10 μg/mL *E. coli* thioredoxin-reductase in 100mM Tris-CI buffer pH 8.0. Either NADH or NADPH was then added to the DTNB reaction as follows:

Reaction A. 200 µM NADPH (Sigma)

Reaction B. 800  $\mu$ M NADH (Sigma)

Reaction C. 800 µM NADH (Roche)

15 Reaction D. (-) cofactor

Reaction E. 800  $\mu$ M NADH (no TR or Trxh).

For the insulin reduction assay, the reaction mixture consisted of 1 mg/mL bovine pancreatic insulin, 20  $\mu$ g/mL *E. coli* thioredoxin, and 20  $\mu$ g/mL *E. coli* thioredoxin-reductase in 100mM potassium phosphate buffer at pH 7.0. Either NADH or NADPH was then added to the reaction as follows:

Reaction A. 800 µM NADPH (Sigma)

Reaction B. 800 µM NADH (Sigma)

Reaction C. 800 µM NADH (Roche)

25 Reaction D. (-) cofactor

20

Reaction E. 2 mM NADH (no TR or Trxh).

The results indicate that NADH, purchased from either Sigma or Roche, could act as an electron donor in both the DTNB and insulin reduction assays.

30 However, the rate of reduction was lower than the rate observed with NADPH as a cofactor. It was estimated that the rate of insulin reduction utilizing NADH as an electron donor was approximately 25-50% when compared to the

-97-

maximum rate using NADPH. Furthermore, it was estimated that the rate of DTNB reduction utilizing NADH as an electron donor was approximately 5-10% of the maximum rate using NADPH. Similar results were observed using the oleosin-thioredoxin-reductase-linker thioredoxin fusion protein on *Arabidopsi*s oil bodies instead of the *E. coli* thioredoxin-reductase and thioredoxin.

## Example 5

Production of multimeric immunoglobulin protein in plant seed cells and capture on oil bodies using Protein A – oleosin fusion proteins.

1 - Production of multimeric immunoglobulin protein in plant seed cells

10

20

25

30

For expression of multimeric-protein-complexes containing multimeric-immunoglobulin-complexes, the cDNA sequences encoding individual light and heavy chains can be isolated from; 1) cell lines expressing a particular antibody, such as clonal B cell lines, or a hybridoma cell line, or 2) may be a recombinant antibody, assembled by combining select light and heavy chain variable domains and available light and heavy chain constant domain sequences, respectively. Variable domains with specific binding properties may be isolated from screening populations of such sequences, usually in the form of a single-chain Fv phage display library.

Starting from known nucleic acid sequences and a source of light and heavy chains, the mature polypeptide coding sequences of each chain is isolated with a secretion signal sequence. The signal sequence can be the native antibody sequence or derived from a known secreted plant sequence (e.g. a PR sequence from Arabidopsis or tobacco). The addition of a plant secretion signal sequence to both light and heavy chain mature coding sequences is carried out by standard molecular biology techniques. PCR fusion is used routinely to make such modifications. Secretion signal sequences are included to target the light and heavy immunoglobulin polypeptides for secretion from the cell and further assembly of the two chains into a multimeric-immunoglobulin-complex. For expression in transgenic plant seeds, an expression cassette is assembled comprising: 1) a regulatory promoter sequence to provide expression in plant seeds, 2) the secretion signal – light chain sequence, and 3) a regulatory

sequence to terminate transcription. A second expression cassette is assembled comprising: 1) a regulatory promoter seguence to provide expression in plant seeds, 2) the secretion signal - heavy chain sequence, and 3) a regulatory sequence to terminate transcription. Each of the antibody chain expression cassettes is cloned individually into an Agrobacterium plant transformation vector or is combined into a single transformation vector with both expression cassettes. In both cases, the expression cassettes are cloned into plant transformation vectors, between the left and right delineating border sequences, and adjacent to a plant selectable marker cassette. Each plant transformation vector is transformed into Agrobacterium. The resulting Agrobacterium strains are used to infect plant tissues. Transgenic plant material is regenerated and viable transgenic plants are selected. When individual transformation vectors are used, the transgenic plant lines that are produced, expressing either light or heavy chain sequences, are crossed to generate a single plant line expressing both chains in the same plant cell. When a single transformation vector, containing both light and heavy expression cassettes, is used, the initial transgenic plant line produces both light and heavy chain sequences in the same plant cell.

10

20

25

30

# 2 - Production of transgenic oil bodies which display Protein A for the capture of immunoglobulins

To capture and display immunoglobulin protein on oil bodies, oil bodies are engineered to display an immunoglobulin binding protein. In this example, the well-known antibody-binding domains from Protein A are used. Based on the known sequence for Protein A from Staphylococcus aureus, PCR primers are designed to isolate the five consecutive Ig-binding domains from the bacterial Protein A sequence. Primers are designed to allow cloning of the Protein A sequence as either an N-terminal or C-terminal fusion to an oleosin sequence for targeting to oil bodies. The sequence that encodes an in-frame translational fusion between Protein A and oleosin is cloned into a plant expression cassette for seed-specific expression. The final cassette consists of a regulatory promoter sequence that provides expression in seeds, the Protein A – oleosin fusion sequence, and a regulatory sequence to terminate transcription. The

Protein A - oleosin expression cassette is cloned into a plant transformation vector compatible with Agrobacterium – mediated plant transformation. The transformation vector comprises left and right border sequences flanking the Protein A – oleosin expression cassette and an adjacent plant selectable marker cassette. The Agrobacterium strain containing this vector is used to infect plant tissues and subsequent regeneration and selection from transgenic plant material to create transgenic plants.

# 3 – Capture and display of multimeric-immunoglobulins on oil bodies displaying Protein A

10

20

25

30

Having produced light and heavy chain multimeric immunoglobulin complexes in one transgenic plant line and the display of Protein A on oil bodies through the oil body targeting of a Protein A – oleosin fusion protein in a second plant line, at least two embodiments can be used to capture the immunoglobulin complex on the Protein A oil bodies. In the first embodiment, transgenic seed from both the immunoglobulin and the Protein A – oleosin expression lines is combined in an optimum ratio and then ground together such that the disrupted material from both seed lines would be combined in the same extract. The combined seed extracts are mixed and/or incubated under conditions that allow maximum recovery of the immunoglobulin by Protein A. The oil body fraction is separated using standard phase separation techniques (e.g. centrifugation). The recovered oil body fraction contains both native oil bodies, from the immunoglobulin expression line, and transgenic Protein A oil bodies from the Protein A – oleosin expression line.

In a second embodiment, the plant lines expressing the immunoglobulin complex and the Protein A – oleosin fusion are crossed and individual plant lines expressing both components are identified and propagated. In this approach, the immunoglobulin complex and the Protein A – oleosin fusion are produced in different cellular compartments of the same plant seed cell. Seed from the double transgenic line is ground to disrupt the cellular material and mix the contents of all cellular compartments, including combining the immunoglobulin in the extracellular compartment and the Protein A – oleosin on the oil body in the cytosolic compartment. The material is mixed and/or incubated under conditions

-100-

to allow maximum recovery of the immunoglobulin by Protein A, and the oil body fraction is separated by phase separation techniques. The recovered oil body fraction contains the displayed Protein A and the capture immunoglobulin complex.

5 Example 6

Production of assembled multimeric-immunoglobulin-complexes as fusions with oil body targeting domains.

Individual polypeptides are produced as a fusion protein with oil body targeting sequences (e.g. oleosin) for display on oil bodies. It has been found that the individual subunits of naturally associating heterodimeric proteins can be co-produced as individual oleosin fusions and still associate as an active heterodimer on the surface of the oil body. In this example, the heterodimer is the light and heavy chain subunits, or derived portions thereof, of an immunoglobulin complex.

15 Production of an immunoglobulin Fab complex on oil bodies.

20

25

30

The mature light chain sequence, lacking the secretion signal sequence, is attached as an in-frame N-terminal fusion to an oleosin sequence. This fusion sequence is assembled into a seed-specific expression cassette consisting of a seed-specific promoter sequence, the light chain – oleosin fusion sequence, and a transcriptional terminator sequence. The expression cassette is inserted between the left and right border markers, adjacent to a plant selectable marker cassette, of a transformation vector. The transformation vector, in Agrobacterium, is used to infect plants and generate transgenic plants.

An equivalent construct for the heavy chain subunit, comprising the variable and constant heavy chain domains, is also attached as an in-frame fusion to oleosin and assembled into an expression cassette for seed-specific expression. The expression cassette can be a part of a separate transformation vector for the generation of a separate transgenic line, or the heavy chain expression cassette can be combined together with the light chain cassette into a single transformation vector. If light and heavy chain expression cassettes are transformed into plants on separate transformation vectors, the individual plant lines are crossed to create a single line expressing both heterodimer subunit —

RECTIFIED SHEET (RULE 91)

-101-

oleosin fusions in the same plant cell. Seed from the double transgenic line, or a single transgenic line generated from the dual expression vector, is extracted to isolate oil bodies. The seed material is ground to release the cellular contents and oil bodies are isolated by phase separation. The targeting of both light and heavy chain sequence to oil bodies, as oleosin fusions, allows the association of the immunoglobulin complex on the surface of the oil body.

Similar configurations, using the entire heavy chain sequence in combination with the entire light chain sequence, or using the variable domains from both the light and heavy chain sequences, are constructed to assemble different types of heteromultimeric-immunoglobulin-complexes (e.g., heterodimers) on the surface of oil bodies.

The present invention should therefore not be seen as limited to the particular embodiments described herein, but rather, it should be understood that the present invention has wide applicability with respect to protein expression generally. Since modifications will be apparent to those of skill in this art, it is intended that this invention be limited only by the scope of the appended claims.

15

-102-

### SUMMARY OF SEQUENCES

SEQ ID NOs:1-4 set forth primers which were synthesized for the isolation of the thioredoxin h (Trxh) and thioredoxin reductase genes from *Arabidopsis*, as described in Example 1.

5

10

20

25

30

SEQ ID NOs:5-7 set forth primers which were designed to code for a specific linker peptide between thioredoxin reductase and thioredoxin proteins, as described in Example 2.

SEQ ID NOs:8, 10 and 11 set forth the nucleotide sequence and the deduced amino acid sequence of the NADPH thioredoxin reductase sequence isolated herein as described in Example 1.

SEQ ID NOs:9 and 11, respectively, set forth the nucleotide sequence of the published NADPH thioredoxin reductase sequence (ATTHIREDB) and the deduced amino acid sequence.

SEQ ID NO:12 sets forth the deduced amino acid sequence of the published NADPH thioredoxin reductase sequence.

SEQ ID NO:13 sets forth the deduced amino acid sequence of the NADPH reductase sequence isolated in this report.

SEQ ID NOs:14 and 15 set forth the nucleotide sequence of the phaseolin promoter-*Arabidopsis* Trxh-phaseolin terminator sequence described in Example 2, and the deduced amino acid sequence. The Trxh coding sequence and its deduced amino acid sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554, and the phaseolin terminator corresponds to nucleotide sequence 1905-3124. The promoter was furnished with a Pstl site (nt 1-6) and the terminator was furnished with a Hindlll site (nt 1898-1903) and a Kpnl site (nt 3124-3129) to facilitate cloning.

SEQ ID NOs:16, 17 and 18 set forth the nucleotide sequence of the phaseolin promoter-oleosin Trxh-phaseolin terminator sequence described in Example 2, and the deduced amino acid sequences. The oleosin-Trxh coding sequence and the deduced amino acid sequences are indicated in SEQ ID NO:16. As in SEQ ID NO:14, the phaseolin promoter corresponds to nucleotide 6-1554.

The sequence encoding cleosin corresponds to nt 1555-2313, the intron in this sequence (nt 1908-2147) is indicated in italics. The Trxh coding sequence

RECTIFIED SHEET (RULE 91)

corresponds to nt 2314-2658. The phaseolin terminator corresponds to nucleotide sequence 2664-3884.

SEQ ID NO:19, 20 and 21 set forth the nucleotide sequence of the phaseolin promoter - Trxh oleosin-phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The Trxh oleosin- coding sequence and its deduced amino acid sequences are indicated in SEQ ID NO:19. As in SEQ ID NOs:14 and 16, the phaseolin promoter corresponds to nucleotide 6-1554. The Trxh coding sequence corresponds to nt 1555-1896. The sequence encoding oleosin corresponds to nt 1897-2658, the intron in this sequence (nt 2250-2489) is indicated in italics. The phaseolin terminator corresponds to nucleotide sequence 2664-3884.

10

20

25

30

SEQ ID NO:22 and 23 set forth the nucleotide sequence of the phaseolin promoter—thioredoxin-reductase-phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequence. The thioredoxin-reductase coding sequence and its deduced amino acid sequence is indicated in SEQ ID NO:22. The phaseolin promoter corresponds to nucleotide 6-1554. The thioredoxin-reductase coding sequence corresponds to nt 1555-2556 and the deduced amino acid is set forth in SEQ ID NO:23. The phaseolin terminator corresponds to nucleotide sequence 2563-3782.

SEQ ID NOs:24, 25 and 26 show the nucleotide sequence of the phaseolin promoter-oleosin thioredoxin-reductase-phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The oleosin-thioredoxin-reductase coding sequence and its deduced amino acid sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554. The sequence encoding oleosin corresponds to nt 1555-2313, the intron in this sequence (nt 1980-2147) is indicated in italics. The thioredoxin-reductase coding sequence corresponds to nt 2314-3315. The phaseolin terminator corresponds to nucleotide sequence 3321-4540.

SEQ ID NOs:27, 28 and 29 show the nucleotide sequence of the phaseolin promoter - thioredoxin-reductase oleosin - phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The thioredoxin-reductase coding sequence and its deduced amino acid

WO 02/50289

10

15

20

25

30

sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554. The thioredoxin-reductase coding sequence corresponds to nt 1555-2553. The sequence encoding oleosin corresponds to nt 2554-3315, the intron in this sequence (nt 2751-3146) is indicated in italics. The phaseolin terminator corresponds to nucleotide sequence 3321-4540.

SEQ ID NO:30, 31 and 32 show the sequence of the phaseolin promoter - oleosin - *Mlep* thioredoxin-reductase/thioredoxin -phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The oleosin-*Mlep* thioredoxin-reductase/thioredoxin coding sequence and its deduced amino acid sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554. The sequence encoding oleosin corresponds to nt 1555-2313, the intron in this sequence (nt) is indicated in italics. The *Mlep* thioredoxin-reductase/thioredoxin coding sequence corresponds to nt 2314-3690. The phaseolin terminator corresponds to nucleotide sequence 3698-4917.

SEQ ID NOs:33, 34 and 35 set forth the nucleotide sequence of the phaseolin promoter-oleosin-thioredoxin-reductase-linker-thioredoxin-phaseolin terminator region of pSBS2542, and the deduced amino acid sequences. The deduced amino acid sequence of oleosin-thioredoxin-reductase-linker-thioredoxin is also shown in SEQ ID NO:33. Amino acids representing oleosin are set forth at positions 1-173, those amino acids representing thioredoxin-reductase are set forth at positions 174-501, those amino acids representing the linker or spacer peptide are set forth at positions 501-524, and those representing thioredoxin are set forth at positions 525-636.

SEQ ID NOs:38 and 39 set forth the nucleotide sequence of Arabidopsis Thaliana Thioredoxin h (Trx h 1) and the encoded protein, respectively.

SEQ ID NOs:40 and 41 set forth the nucleotide sequence of Arabidopsis Thaliana Thioredoxin Reductase (NTR1) and the encoded protein, respectively.

SEQ ID NOs:42 and 43 set forth the nucleotide sequence of E. Coli Thioredoxin (TrxA) and the encoded protein, respectively.

SEQ ID NOs:44 and 45, set forth the nucleotide sequence of E. Coli Thioredoxin Reductase and the encoded protein, respectively.

PCT/US01/50240 WO 02/50289

-105-

SEQ ID NOs:46 and 47 set forth the nucleotide sequence of Human Thioredoxin and the encoded protein, respectively.

SEQ ID NOs:48 and 49, set forth the nucleotide sequence of Human Thioredoxin Reductase and the encoded protein, respectively.

SEQ ID NOs:50 and 51, respectively, set forth the nucleotide sequence of Mycobacterium leprae Thioredoxin-Thioredoxin Reductase and the encoded protein, respectively.

SEQ ID NOs:52-313 are described in Table 5.

# **TABLE 5**

10

5

| SEQ. ID                    | SWISS PROTEIN IDENTIFIER   |  |  |  |
|----------------------------|--|--|--|--|
|                            | (in parenthesis)   |  |  |  |
| EXAMPLES OF REDOX PROTEINS |  |  |  |  |
| PLANT THIOREDOXINS         |  |  |  |  |
|                            | Thioredoxin f-type   |  |  |  |
| 52                         | (Q9XFH8) Thioredoxin F-type 1, chloroplast precursor (TRX-F1) Arabidopsis thaliana (Mouse-ear cress)   |  |  |  |
| 53                         | (Q9XFH9) Thioredoxin F-type 2, chloroplast precursor (TRX-F2). {GENE: AT5G16400 OR MQK4.13} - Arabidopsis thalians (Mouse-ear cress)             |  |  |  |
| 54                         | (O48897) Thioredoxin F-type, chloroplast precursor (TRX-F). {GENE: TRXF} - Brassica napus (Rape)   |  |  |  |
| 55                         | (081332) Thioredoxin F-type, chloroplast precursor (TRX-F) Mesembryanthemum crystallinum (Common ice plant)                                      |  |  |  |
| 56                         | (P29450) Thioredoxin F-type, chloroplast precursor (TRX-F) Pisum sativum (Garden pea)  |  |  |  |
| 57                         | (P09856) Thioredoxin F-type, chloroplast precursor (TRX-F) Spinacia oleracea (Spinach)   |  |  |  |
|                            | Thioredoxin m-type   |  |  |  |
| 58                         | (P06544) Thioredoxin 1 (TRX-1) (Thioredoxin M). {GENE: TRXA} - Anabaena sp. (strain PCC 7119)  |  |  |  |
| 59                         | (O48737) Thioredoxin M-type 1, chloroplast precursor (TRX-M1). {GENE: AT1G03680 OR F21B7_7 OR F21B7.28} - Arabidopsis thaliana (Mouse-ear cress) |  |  |  |

2

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----------------|---|
|                | EXAMPLES OF REDOX PROTEINS  |
| 60             | (Q9SEU8) Thioredoxin M-type 2, chloroplast precursor (TRX-M2). {GENE: AT4G03520 OR F9H3.15 OR T5L23.1} - Arabidopsis thaliana (Mouse-ear cress) |
| 61             | (Q9SEU7) Thioredoxin M-type 3, chloroplast precursor (TRX-M3). {GENE: AT2G15570 OR F9O13.12} - Arabidopsis thaliana (Mouse-ear cress)           |
| 62             | (Q9SEU6) Thioredoxin M-type 4, chloroplast precursor (TRX-M4) Arabidopsis thaliana (Mouse-ear cress)  |
| 63             | (Q9XGS0) Thioredoxin M-type, chloroplast precursor (TRX-M) Brassica napus (Rape)  |
| 64             | (P23400) Thioredoxin M-type, chloroplast precursor (TRX-M) (Thioredoxin CH2). {GENE: TRXM} - Chlamydomonas reinhardtii                          |
| 65             | (Q41864) Thioredoxin M-type, chloroplast precursor (TRX-M). {GENE: TRM1} - Zea mays (Maize)   |
| 66             | (Q9ZP20) Thioredoxin M-type, chloroplast precursor (TRX-M) Oryza sativa (Rice)  |
| 67             | (P48384) Thioredoxin M-type, chloroplast precursor (TRX-M) Pisum sativum (Garden pea)   |
| 68             | (P07591) Thioredoxin M-type, chloroplast precursor (TRX-M) Spinacia oleracea (Spinach)  |
| 69             | (Q9ZP21) Thioredoxin M-type, chloroplast precursor (TRX-M) Triticum aestivum (Wheat)  |
| 70             | (P12243) Thioredoxin 1 (TRX-1) (Thioredoxin M). {GENE: TRXA OR TRXM} - Synechococcus sp. (strain PCC 7942) (Anacystis nidulans R2)              |
| 71             | (P37395) Thioredoxin. {GENE: TRXA OR TRX} - Cyanidium caldarium [Chloroplast]   |
| 72             | (O22022) Thioredoxin. {GENE: TRXA OR TRXM} - Cyanidioschyzon merolae [Chloroplast]  |
| 73             | (P50338) Thioredoxin. {GENE: TRXA} - Griffithsia pacifica [Chloroplast]   |

| SEQ. ID<br>NO | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|---------------|---|
|               | EXAMPLES OF REDOX PROTEINS  |
| 74            | (P50254) Thioredoxin. {GENE: TRXA} - Porphyra yezoensis [Chloroplast]   |
| 75            | (P51225) Thioredoxin. {GENE: TRXA} - Porphyra purpurea [Chloroplast]  |
|               | Thioredoxin h-type  |
| 76            | (P29448) Thioredoxin H-type 1 (TRX-H-1). {GENE: TRX1 OR AT3G51030 OR F24M12.70} - Arabidopsis thaliana (Mouse-ear cress)                        |
| 77            | (P20857) Thioredoxin 2 (TRX-2). {GENE: TRXB} - Anabaena sp. (strain PCC 7120)   |
| 78            | (Q42388) Thioredoxin H-type 1 (TRX-H-1) (Pollen coat protein). {GENE: THL-1 OR BOPC17} - Brassica napus (Rape), Brassica oleracea (Cauliflower) |
| 79            | (P29449) Thioredoxin H-type 1 (TRX-H1) Nicotiana tabacum (Common tobacco)   |
| 80            | (Q38879) Thioredoxin H-type 2 (TRX-H-2). {GENE: TRX2 OR AT5G39950 OR MYH19.14} - Arabidopsis thaliana (Mouse-ear cress)                         |
| 81            | (Q39362) Thioredoxin H-type 2 (TRX-H-2). {GENE: THL-2} - Brassica napus (Rape)  |
| 82            | (Q07090) Thioredoxin H-type 2 (TRX-H2) Nicotiana tabacum (Common tobacco)   |
| 83            | (Q42403) Thioredoxin H-type 3 (TRX-H-3). {GENE: TRX3 OR AT5G42980 OR MBD2.18} - Arabidopsis thaliana (Mouse-ear cress)                          |
| 84            | (Q39239) Thioredoxin H-type 4 (TRX-H-4). {GENE: TRX4} - Arabidopsis thaliana (Mouse-ear cress)  |
| 85            | (Q39241) Thioredoxin H-type 5 (TRX-H-5). {GENE: TRX5} - Arabidopsis thaliana (Mouse-ear cress)  |
| 86            | (O64432) Thioredoxin H-type (TRX-H). {GENE: PEC-2} - Brassica rapa (Turnip)   |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |
|----------------|--|
|                | EXAMPLES OF REDOX PROTEINS   |
| 87             | (P80028) Thioredoxin H-type (TRX-H) (Thioredoxin CH1). {GENE: TRXH} - Chlamydomonas reinhardtii  |
| 88             | (Q96419) Thioredoxin H-type (TRX-H) Fagopyrum esculentum (Common buckwheat)  |
| 89             | (Q42443) Thioredoxin H-type (TRX-H) (Phloem sap 13 kDa protein-1) Oryza sativa (Rice)  |
| 90             | (O65049) Thioredoxin H-type (TRX-H). {GENE: SB09} - Picea mariana (Black spruce)   |
| 91             | (Q43636) Thioredoxin H-type (TRX-H) Ricinus communis (Castor bean)   |
| 92             | (064394) Thioredoxin H-type (TRX-H) (TrxTa) Triticum aestivum (Wheat)  |
| 93             | (P29429) Thioredoxin Emericella nidulans (Aspergillus nidulans)  |
| VIRUSES, E     | BACTERIA AND FUNGI THIOREDOXINS  |
| 94             | (P80579) Thioredoxin (TRX). {GENE: TRXA} - Alicyclobacillus acidocaldarius (Bacillus acidocaldarius)   |
| 95             | (O28137) Thioredoxin. {GENE: AF2145} - Archaeoglobus fulgidus  |
| 96             | (P14949) Thioredoxin (TRX). {GENE: TRXA OR TRX} - Bacillus subtilis  |
| 97             | (P00276) Thioredoxin. {GENE: NRDC} - Bacteriophage T4  |
| 98             | (O51088) Thioredoxin (TRX). {GENE: TRXA OR BB0061} - Borrelia burgdorferi (Lyme disease spirochete)  |
| 99             | (P57653) Thioredoxin (TRX). {GENE: TRXA OR BU597} - Buchnera aphidicola (subsp. Acyrthosiphon pisum) (Acyrthosiphon pisum symbiotic bacterium) |
| 100            | (051890) Thioredoxin (TRX). {GENE: TRXA} - Buchnera aphidicola (subsp. Schizaphis graminum)  |
| 101            | (P10472) Thioredoxin (TRX). {GENE: TRXA} - Chlorobium limicola f.sp. thiosulfatophilum   |

10

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----------------|---|
|                | EXAMPLES OF REDOX PROTEINS  |
| 102            | (Q9PJK3) Thioredoxin (TRX). {GENE: TRXA OR TC0826} - Chlamydia muridarum  |
| 103            | (Q9Z7P5) Thioredoxin (TRX). {GENE: TRXA OR CPN0659 OR CP0088} - Chlamydia pneumoniae (Chlamydophila pneumoniae)       |
| 104            | (P52227) Thioredoxin (TRX). {GENE: TRXA} - Chlamydia psittaci (Chlamydophila psittaci)                                |
| 105            | (O84544) Thioredoxin (TRX). {GENE: TRXA OR CT539} - Chlamydia trachomatis   |
| 106            | (P00275) Thioredoxin C-1 Corynebacterium nephridii  |
| 107            | (P07887) Thioredoxin C-2 Corynebacterium nephridii  |
| 108            | (P52228) Thioredoxin C-3 Corynebacterium nephridii  |
| 109            | (P09857) Thioredoxin (TRX). {GENE: TRXA} - Chromatium vinosum   |
| 110            | (P21609) Thioredoxin (TRX). {GENE: TRXA} - Clostridium litorale (Bacterium W6)  |
| 111            | (P81108) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Clostridium sporogenes  |
| 112            | (P81109) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Clostridium sticklandii   |
| 113            | (Q9UW02) Thioredoxin (Allergen Cop c 2) Coprinus comatus (Shaggy mane)  |
| 114            | (P29445) Thioredoxin 1. {GENE: TRXA OR TRX1} - Dictyostelium discoideum (Slime mold)                                  |
| 115            | (P29446) Thioredoxin 2 (Fragment). {GENE: TRXB OR TRX2} - Dictyostelium discoideum (Slime mold)                       |
| 116            | (P29447) Thioredoxin 3. {GENE: TRXC OR TRX3} - Dictyostelium discoideum (Slime mold)                                  |
| 117            | (P00274) Thioredoxin 1 (TRX1) (TRX). {GENE: TRXA OR TSNC OR FIPA OR B3781} - Escherichia coli, Salmonella typhimurium |

10

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |
|----------------|--|
|                | EXAMPLES OF REDOX PROTEINS   |
| 118            | (P52232) Thioredoxin-like protein SLR0233. {GENE: SLR0233} - Synechocystis sp. (strain PCC 6803)   |
| 119            | (P33636) Thioredoxin 2 (Trx2). {GENE: TRXC OR B2582 OR Z3867 OR ECS3448} - Escherichia coli, Escherichia coli O157:H7  |
| 120            | (P21610) Thioredoxin (TRX). {GENE: TRXA} - Eubacterium acidaminophilum   |
| 121            | (P43785) Thioredoxin (TRX). {GENE: TRXA OR TRXM OR HI0084} - Haemophilus influenzae  |
| 122            | (P43787) Thioredoxin-like protein HI1115. {GENE: HI1115} - Haemophilus influenzae  |
| 123            | (P56430) Thioredoxin (TRX). {GENE: TRXA OR HP0824 OR JHP0763} - Helicobacter pylori (Campylobacter pylori), Helicobacter pylori J99 (Campylobacter pylori J99)                     |
| 124            | (Q9S386) Thioredoxin (EC 1.6.4.5) {GENE:TRXA} - Listeria monocytogenes   |
| 125            | (Q57755) Thioredoxin. {GENE: TRX OR MJ0307} - Methanococcus jannaschii   |
| 126            | (P47370) Thioredoxin (TRX). {GENE: TRXA OR TRX OR MG124} - Mycoplasma genitalium   |
| 127            | (P46843) Bifunctional thioredoxin-reductase/thioredoxin [Includes: Thioredoxin-reductase (EC 1.6.4.5) (TRXR); Thioredoxin]. {GENE: TRXB/A OR TRX OR ML2703} - Mycobacterium leprae |
| 128            | (P75512) Thioredoxin (TRX). {GENE: TRXA OR TRX OR MPN263 OR MP570} - Mycoplasma pneumoniae   |
| 129            | (030974) Thioredoxin (TRX). {GENE: TRXA} - Mycobacterium smegmatis   |
| 130            | (P52229) Thioredoxin (TRX) (MPT46). {GENE: TRXA OR TRX OR TRXC OR RV3914 OR MT4033 OR MTV028.05} - Mycobacterium tuberculosis  |
| 131            | (P42115) Thioredoxin. {GENE: TRX} - Neurospora crassa  |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----------------|---|
| 3.7            | EXAMPLES OF REDOX PROTEINS  |
| 132            | (P34723) Thioredoxin. {GENE: TRXA} - Penicillium chrysogenum                                      |
| 133            | (Q9X2T1) Thioredoxin (TRX). {GENE: TRXA OR TRX OR PA5240} - Pseudomonas aeruginosa                |
| 134            | (P10473) Thioredoxin (TRX). {GENE: TRXA} - Rhodospirillum rubrum                                  |
| 135            | (P08058) Thioredoxin (TRX). {GENE: TRXA} - Rhodobacter sphaeroides (Rhodopseudomonas sphaeroides) |
| 136            | (Q9ZEE0) Thioredoxin (TRX). {GENE: TRXA OR RP002} - Rickettsia prowazekii                         |
| 137            | (P33791) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Streptomyces aureofaciens                   |
| 138            | (P52230) Thioredoxin (TRX). {GENE: TRXA OR SCH24.11C} - Streptomyces coelicolor                   |
| 139            | (Q05739) Thioredoxin (TRX). {GENE: TRXA} - Streptomyces clavuligerus                              |
| 140            | (P52231) Thioredoxin (TRX). {GENE: TRXA OR SLR0623} - Synechocystis sp. (strain PCC 6803)         |
| 141            | (P73263) Thioredoxin-like protein SLR1139. {GENE: SLR1139} - Synechocystis sp. (strain PCC 6803)  |
| 142            | (P52233) Thioredoxin (TRX). {GENE: TRXA} - Thiobacillus ferrooxidans                              |
| 143            | (P96132) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Thiocapsa roseopersicina                    |
| 144            | (P81110) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Tissierella creatinophila                   |
| 145            | (083889) Thioredoxin (TRX). {GENE: TRXA OR TP0919} - Treponema pallidum                           |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----------------|---|
|                | EXAMPLES OF REDOX PROTEINS  |
| ANIMAL TH      | IIOREDOXIN  |
| 146            | (097680) Thioredoxin. {GENE: TXN} - Bos taurus (Bovine)   |
| 147            | (Q95108) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Bos taurus (Bovine)  |
| 148            | (Q09433) Thioredoxin. {GENE: B0228.5} - Caenorhabditis elegans  |
| 149            | (P99505) Thioredoxin (Fragment). {GENE: TXN} - Canis familiaris (Dog  |
| 150            | (P08629) Thioredoxin. {GENE: TXN} - Gallus gallus (Chicken)   |
| 151            | (P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly)  |
| 152            | (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRDX OR TRX} - Homo sapiens (Human) |
| 153            | (Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human)   |
| 154            | (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhesumacaque)   |
| 155            | (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse)   |
| 156            | (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse)   |
| 157            | (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig)   |
| 158            | (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit)  |
| 159            | (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat  |
| 160            | (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)  |
| 161            | (P50413) Thioredoxin. {GENE: TXN} - Ovis aries (Sheep)  |

5

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----------------|---|
|                | EXAMPLES OF REDOX PROTEINS  |
| 162            | (O23166) THIOL-DISULFIDE INTERCHANGE LIKE PROTEIN (THIOREDOXIN-LIKE PROTEIN) {GENE:C7A10.160 OR AT4G37200 OR HCF164} - Arabidopsis thaliana (Mouse-ear cress) |
| 163            | (Q9C9Y6) Thioredoxin-like protein {GENE:F17O14.18} - Arabidopsis thaliana (Mouse-ear cress)   |
| 164            | (Q9FYD5) Thioredoxin-like protein {GENE:F21E1_180} - Arabidopsis thaliana (Mouse-ear cress)   |
| 165            | (Q38878) THIOREDOXIN-LIKE PROTEIN {GENE:TRX6 OR T7D17.3} - Arabidopsis thaliana (Mouse-ear cress)   |
| 166            | (Q9LVI2) Thioredoxin-like protein - Arabidopsis thaliana (Mouse-ear cress)  |
| 167            | (Q9SCN9) Thioredoxin-like protein {GENE:T4D2.150} -<br>Arabidopsis thaliana (Mouse-ear cress)   |
| 168            | (Q9SRD7) Thioredoxin-like protein, 49720-48645<br>(GENE:F28016.13) - Arabidopsis thaliana (Mouse-ear cress)   |
| 169            | (Q9SU84) THIOREDOXIN-LIKE PROTEIN {GENE:T16L4.180 OR AT4G29670} - Arabidopsis thaliana (Mouse-ear cress)  |
| 170            | (Q9SWG6) Thioredoxin-like protein {GENE:TRX} - Hordeum bulbosum   |
| 171            | (Q9SWG4) Thioredoxin-like protein {GENE:TRX} - Lolium perenne (Perennial ryegrass)  |
| 172            | (Q9AS75) Thioredoxin-like protein {GENE:P0028E10.17} - Oryza sativa (Rice)  |
| 173            | (004002) CDSP32 protein (Chloroplast Drought-induced Stress<br>Protein of 32kDa) - Solanum tuberosum (Potato)   |
| 174            | (Q9SWG5) Thioredoxin-like protein {GENE:TRX} - Secale cereale (Rye)   |
| 175            | (Q9SP36) Thioredoxin-like protein (Fragment) {GENE:TRX} - Secale cereale (Rye)  |
| 176            | (Q9U515) Thioredoxin-like protein - Manduca sexta (Tobacco hawkmoth) (Tobacco hornworm)   |

-114-

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |  |  |
|----------------|--|--|--|
|                | EXAMPLES OF REDOX PROTEINS   |  |  |
| VIRUSES, B     | ACTERIA AND FUNGI THIOREDOXIN-LIKE PROTEINS  |  |  |
| 177            | (P43221) Thiol:disulfide interchange protein tlpA (Cytochrome c biogenesis protein tlpA). {GENE: TLPA} - Bradyrhizobium japonicum                                      |  |  |
| 178            | (P43787) Thioredoxin-like protein HI1115. {GENE: HI1115} - Haemophilus influenzae  |  |  |
| 179            | (Q9GUP7) Thioredoxin-like protein {GENE:TRXLP} - Leishmani<br>major  |  |  |
| 180            | (Q9UVH0) Thioredoxin-like protein - Mortierella alpina   |  |  |
| 181            | (P95355) Thioredoxin-like protein - Neisseria gonorrhoeae  |  |  |
| 182            | (Q98G37) Thioredoxin-like protein {GENE:MLL3505} -<br>Rhizobium loti (Mesorhizobium loti)  |  |  |
| 183            | (P36893) Thiol:disulfide interchange protein helX precursor (Cytochrome c biogenesis protein helX). {GENE: HELX} - Rhodobacter capsulatus (Rhodopseudomonas capsulata) |  |  |
| 184            | (P52232) Thioredoxin-like protein SLR0233, {GENE: SLR0233 - Synechocystis sp. (strain PCC 6803)  |  |  |
| 185            | (P73263) Thioredoxin-like protein SLR1139. {GENE: SLR1139 - Synechocystis sp. (strain PCC 6803)  |  |  |
| 186            | (Q9USR1) Thioredoxin-like protein {GENE:SPBC577.08C} - Schizosaccharomyces pombe (Fission yeast)   |  |  |
| 187            | (Q9R788) Thioredoxin {GENE:TPTRX} - Treponema pallidum   |  |  |
| ANIMALS T      | HIOREDOXIN-LIKE PROTEINS   |  |  |
| 188            | (Q9UAV4) F46E10.9 PROTEIN (THIOREDOXIN-LIKE PROTEIN DPY-11) {GENE:F46E10.9 OR DPY-11} - Caenorhabditis elegans   |  |  |
| 189            | (Q9N2K6) Thioredoxin-like protein (Y54E10A.3 protein)<br>(Thioredoxin-like protein TXL) {GENE:TXL QR Y54E10A.3} -<br>Caenorhabditis elegans                            |  |  |
| 190            | (Q9VRP3) THIOREDOXIN-LIKE PROTEIN TXL (CG5495 PROTEIN) {GENE:TXL OR CG5495} - Drosophila melanogaster (Fruit fly)  |  |  |

5

10

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----------------|---|
|                | EXAMPLES OF REDOX PROTEINS  |
| 191            | (O43396) Thioredoxin-like protein (32 kDa thioredoxin-related protein). {GENE: TXNL OR TRP32 OR TXL} - Homo sapiens (Human)   |
| 192            | (O76003) Thioredoxin-like protein - Homo sapiens (Human)  |
| 193            | (Q9S753) THIOREDOXIN-LIKE PROTEIN {GENE:TRX} - Phalaris coerulescens  |
| 194            | (O77404) TRYPAREDOXIN - Trypanosoma brucei brucei   |
| PLANT TH       | OREDOXIN-REDUCTASES   |
| 195            | (Q39243) Thioredoxin-reductase 1 (EC 1.6.4.5) (NADPH-dependent thioredoxin-reductase 1) (NTR 1). {GENE: NTR1 OR AT4G35460 OR F15J1.30} - Arabidopsis thaliana (Mouse-ear cress) |
| 196            | (Q39242) Thioredoxin-reductase 2 (EC 1.6.4.5) (NADPH-dependent thioredoxin-reductase 2) (NTR 2). {GENE: NTR2 OR AT2G17420 OR F5J6.18} - Arabidopsis thaliana (Mouse-ear cress)  |
| VIRUSES, E     | BACTERIA AND FUNGI THIOREDOXIN-REDUCTASES   |
| 197            | (O66790) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR AQ_500} - Aquifex aeolicus   |
| 198            | (P80880) Thioredoxin-reductase (EC 1.6.4.5) (TRXR) (General stress protein 35) (GSP35). {GENE: TRXB} - Bacillus subtilis  |
| 199            | (P94284) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR BB0515} - Borrelia burgdorferi (Lyme disease spirochete)   |
| 200            | (P57399) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR BU314} - Buchnera aphidicola (subsp. Acyrthosiphon pisum) (Acyrthosiphon pisum symbiotic bacterium)          |
| 201            | (P81433) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Buchnera aphidicola (subsp. Schizaphis graminum)   |
| 202            | (Q9PKT7) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR TC0375} - Chlamydia muridarum  |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |
|----------------|--|
|                | EXAMPLES OF REDOX PROTEINS   |
| 203            | (Q9Z8M4) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR CPN0314 OR CP0444} - Chlamydia pneumoniae (Chlamydophila pneumoniae)  |
| 204            | (O84101) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR CT099} - Chlamydia trachomatis  |
| 205            | (P52213) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Clostridium litorale (Bacterium W6)   |
| 206            | (P39916) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Coxiella burnetii   |
| 207            | (P09625) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR B0888 OR Z1232 OR ECS0973} - Escherichia coli, Escherichia coli O157:H7   |
| 208            | (P50971) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Eubacterium acidaminophilum   |
| 209            | (P43788) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR HI1158} - Haemophilus influenzae  |
| 210            | (Q9ZL18) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR JHP0764} - Helicobacter pylori J99 (Campylobacter pylori J99)   |
| 211            | (P56431) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR HP0825} - Helicobacter pylori (Campylobacter pylori)  |
| 212            | (O32823) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR LMO2478} - Listeria monocytogenes   |
| 213            | (P47348) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR MG102} - Mycoplasma genitalium  |
| 214            | (P46843) Bifunctional thioredoxin-reductase/thioredoxin [Includes: Thioredoxin-reductase (EC 1.6.4.5) (TRXR); Thioredoxin]. {GENE: TRXB/A OR TRX OR ML2703} - Mycobacterium leprae |
| 215            | (P75531) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). (GENE: TRXB OR MPN240 OR MP591) - Mycoplasma pneumonjae  |
| 216            | (O30973) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Mycobacterium smegmatis   |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |
|----------------|--|
|                | EXAMPLES OF REDOX PROTEINS   |
| 217            | (P52214) Thioredoxin-reductase (EC 1.6.4.5) (TRXR) (TR). {GENE: TRXB OR RV3913 OR MT4032 OR MTV028.04} - Mycobacterium tuberculosis        |
| 218            | (P51978) Thioredoxin-reductase (EC 1.6.4.5). {GENE: CYS-9} - Neurospora crassa   |
| 219            | (P43496) Thioredoxin-reductase (EC 1.6.4.5). {GENE: TRXB} - Penicillium chrysogenum  |
| 220            | (Q9ZD97) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR RP445} - Rickettsia prowazekii  |
| 221            | (Q92375) Thioredoxin-reductase (EC 1.6.4.5). {GENE: SPBC3F6.03} - Schizosaccharomyces pombe (Fission yeast)                                |
| 222            | (Q05741) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Streptomyces clavuligerus   |
| 223            | (P52215) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR SCH24.12} - Streptomyces coelicolor                                     |
| 224            | (083790) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR TP0814} - Treponema pallidum  |
| 225            | (P80892) Thioredoxin-reductase (EC 1.6.4.5) (TRXR) (Fragment). {GENE: TRXB} - Vibrio fischeri  |
| 226            | (P29509) Thioredoxin-reductase 1 (EC 1.6.4.5). {GENE: TRR1 OR YDR353W OR D9476.5} - Saccharomyces cerevisiae (Baker's yeast)               |
| 227            | (P38816) Thioredoxin-reductase 2, mitochondrial precursor (EC 1.6.4.5). {GENE: TRR2 OR YHR106W} - Saccharomyces cerevisiae (Baker's yeast) |
| ANIMAL TH      | IIOREDOXIN-REDUCTASES  |
| 228            | (O62768) Thioredoxin-reductase (EC 1.6.4.5). {GENE: TXNRD1} - Bos taurus (Bovine)  |
| 229            | (Q17745) Thioredoxin-reductase (EC 1.6.4.5). {GENE: C06G3.7} - Caenorhabditis elegans  |
| 230            | (Q16881) Thioredoxin-reductase (EC 1.6.4.5). {GENE: TXNRD1} - Homo sapiens (Human)   |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |  |  |
|----------------|--|--|--|
|                | EXAMPLES OF REDOX PROTEINS   |  |  |
| 231            | (Q25861) Thioredoxin-reductase (EC 1.6.4.5) (TrxR). (GENE: TR OR GR) - Plasmodium falciparum (isolate FCH-5) |  |  |
|                | Other thioredoxin-reductases   |  |  |
| PLANTS TH      | IIOREDOXIN-REDUCTASES  |  |  |
| 232            | (O22229) Thioredoxin-reductase {GENE:AT2G41680} - Arabidopsis thaliana (Mouse-ear cress)                     |  |  |
| 233            | (Q39951) NADPH thioredoxin-reductase (Fragment) - Helianthus annuus (Common sunflower)                       |  |  |
| VIRUSES, E     | ACTERIA AND FUNGI THIOREDOXIN-REDUCTASES   |  |  |
| 234            | (O28718) THioredoxin-reductase (TRXB) {GENE:AF1554} - Archaeoglobus fulgidus                                 |  |  |
| 235            | (Q9K703) Thioredoxin-reductase (NADPH) (EC 1.6.4.5) {GENE:TRXB OR BH3571} - Bacillus halodurans              |  |  |
| 236            | (Q9K7F3) Thioredoxin-reductase {GENE:BH3408} - Bacillus halodurans   |  |  |
| 237.           | (Q9KCZ0) Thioredoxin-reductase {GENE:BH1429} - Bacillus halodurans   |  |  |
| 238            | (Q9KCZ1) Thioredoxin-reductase {GENE:BH1428} - Bacillus halodurans   |  |  |
| 239            | (Q9PIY1) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB OF CJ0146} - Campylobacter jejuni                     |  |  |
| 240            | (Q9A4G3) Thioredoxin-reductase {GENE:CC2871} - Caulobacter crescentus  |  |  |
| 241            | (Q97EM8) Thioredoxin-reductase {GENE:CAC3082} - Clostridium acetobutylicum                                   |  |  |
| 242            | (Q97IU2) Thioredoxin-reductase {GENE:CAC1548} - Clostridium acetobutylicum                                   |  |  |
| 243            | (Q9EV96) Thioredoxin-reductase {GENE:TRXB} - Clostridium sticklandii   |  |  |
| 244            | (Q9RSY7) THioredoxin-reductase {GENE:DR1982} - Deinococcus radiodurans                                       |  |  |

10

|    | SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |
|----|----------------|--|
|    |                | EXAMPLES OF REDOX PROTEINS   |
|    | 245            | (O30739) Thioredoxin-reductase (Fragment) - Enterococcus faecalis (Streptococcus faecalis)   |
|    | 246            | (054535) Thioredoxin-reductase {GENE:TRXB OR TRXB1_2 OR VNG6452G OR TRXB1_1 OR VNG6074G} - Halobacterium sp. (strain NRC-1) [Plasmid pNRC100, and Plasmid pNRC200] |
|    | 247            | (P82854) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB2} - Halobacterium sp. (strain NRC-1)  |
|    | 248            | (Q9HN08) Thioredoxin-reductase {GENE:TXRB3 OR VNG2301G} - Halobacterium sp. (strain NRC-1)   |
| 5  | 249            | (O25779) THioredoxin-reductase (TRXB) {GENE:HP1164} - Helicobacter pylori (Campylobacter pylori)   |
|    | 250            | (O86255) Thioredoxin-reductase {GENE:TRXB} - Klebsiella oxytoca  |
|    | 251            | (Q9AEV9) Thioredoxin-reductase (Fragment) {GENE:TRXB} - Lactococcus lactis (subsp. lactis) (Streptococcus lactis)  |
|    | 252            | (Q9CF34) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB2} - Lactococcus lactis (subsp. lactis) (Streptococcus lactis)   |
|    | 253            | (Q9CH02) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB1} - Lactococcus lactis (subsp. lactis) (Streptococcus lactis)   |
| 10 | 254            | (Q9ZFC8) Thioredoxin-reductase (Fragment) {GENE:TRXB} - Lactococcus lactis   |
|    | 255            | (O32822) Hypothetical 39.7 kDa protein (Fragment) - Listeria monocytogenes   |
|    | 256            | (O26804) THioredoxin-reductase {GENE:MTH708} - Methanothermobacter thermautotrophicus  |
|    | 257            | (P94397) Homologue of thioredoxin-reductase of Mycoplama genitalium {GENE:YCGT} - Bacillus subtilis  |
|    | 258            | (Q98PK9) THioredoxin-reductase (EC 1.6.4.5) {GENE:MYPU_7130} - Mycoplasma pulmonis   |
| 15 | 259            | (Q9JU23) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB OR NMA1538} - Neisseria meningitidis (serogroup A)  |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |  |
|----------------|--|--|
|                | EXAMPLES OF REDOX PROTEINS   |  |
| 260            | (Q9JZ28) Thioredoxin-reductase {GENE:NMB1324} - Neisseria meningitidis (serogroup B)         |  |
| 261            | (Q9I0M2) Thioredoxin-reductase 1 {GENE:TRXB1 OR PA2616} - Pseudomonas aeruginosa .           |  |
| 262            | (Q9I592) Thioredoxin-reductase 2 {GENE:TRXB2 OR PA0849} - Pseudomonas aeruginosa             |  |
| 263            | (Q9V0Q8) THioredoxin-reductase (TRXB) {GENE:TRXB OR PAB0500} - Pyrococcus abyssi             |  |
| 264            | (Q9ZD33) THioredoxin-reductase (TRXB2) {GENE:RP514} - Rickettsia prowazekii                  |  |
| 265            | ( <b>054079</b> ) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB} - Staphylococcus aureus     |  |
| 266            | (Q9RIS2) Thioredoxin-reductase {GENE:TRXB OR TRXB2} - Streptomyces coelicolor                |  |
| 267            | (Q9K4L6) Thioredoxin-reductase {GENE:SC5F8.08C} - Streptomyces coelicolor                    |  |
| 268            | (Q97PY2) Thioredoxin-reductase {GENE:SP1458} -<br>Streptococcus pneumoniae                   |  |
| 269            | (Q9A0B5) Thioredoxin-reductase {GENE:SPY0850} - Streptococcus pyogenes                       |  |
| 270            | (Q97V69) Thioredoxin-reductase (trxB-2) (EC 1.6.4.5) {GENE:TRXB-2} - Sulfolobus solfataricus |  |
| 271            | (Q97W27) Thioredoxin-reductase (trxB-3) (EC 1.6.4.5) {GENE:TRXB-3} - Sulfolobus solfataricus |  |
| 272            | (Q97WJ5) Thioredoxin-reductase (trxB-1) (EC 1.6.4.5) {GENE:TRXB-1} - Sulfolobus solfataricus |  |
| 273            | (Q98I59) Thioredoxin-reductase {GENE:MLL2552} - Rhizobium loti (Mesorhizobium loti)          |  |
| . 274          | (Q98M06) Thioredoxin-reductase {GENE:MLL0792} -<br>Rhizobium loti (Mesorhizobium loti)       |  |

10

PCT/US01/50240 WO 02/50289

-121-

|    | SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----|----------------|---|
|    |                | EXAMPLES OF REDOX PROTEINS  |
|    | 275            | (Q9UR80) 35 kDa THioredoxin-reductase HOMOLOG (FRAGMENT) {GENE:TRR1 AND YDR353W} - Saccharomyces cerevisiae (Baker's yeast) |
|    | 276            | (Q9ZEH4) THIOREDOXIN {GENE:TRXA OR SA0992} - Staphylococcus aureus, Staphylococcus aureus subsp. aureus N315                |
|    | 277            | (Q9S1H1) Thioredoxin-reductase (Fragment) {GENE:TRXB} - Staphylococcus xylosus  |
|    | 278            | (Q9HJI4) Thioredoxin-reductase {GENE:TA0984} - Thermoplasma acidophilum   |
| 5  | 279            | (Q9WZX3) Thioredoxin-reductase {GENE:TM0869} - Thermotoga maritima  |
|    | 280            | (Q979K8) Thioredoxin-reductase {GENE:TVG1183005} - Thermoplasma volcanium   |
|    | 281            | (Q9PR71) Thioredoxin-reductase {GENE:TRXB OR UU074} - Ureaplasma parvum (Ureaplasma urealyticum biotype 1)                  |
|    | 282            | (Q9KSS4) Thioredoxin-reductase {GENE:VC1182} - Vibrio cholerae  |
|    | 283            | (Q9PDD1) Thioredoxin-reductase {GENE:XF1448} - Xylella fastidiosa   |
| 10 | 284            | (Q9X5F7) Thioredoxin-reductase {GENE:TRXB1} - Zymomonas mobilis   |
|    | ANIMAL TH      | HOREDOXIN-REDUCTASES  |
|    | 285            | (Q9GKW9) Thioredoxin-reductase 3 (Fragment) {GENE:TRXR3} - Bos taurus (Bovine)  |
|    | 286            | (Q9N2I8) Thioredoxin-reductase (EC 1.6.4.5) - Bos taurus (Bovine)   |
|    | 287            | (Q9N2K1) Thioredoxin-reductase homolog - Caenorhabditis elegans   |
| 15 | 288            | (Q9NJH3) Thioredoxin-reductase - Caenorhabditis elegans   |

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)   |
|----------------|---|
| ·              | EXAMPLES OF REDOX PROTEINS  |
| 289            | (Q9VNT5) CG11401 PROTEIN (THioredoxin-reductase 2) {GENE:TRXR-2 OR CG11401} - Drosophila melanogaster (Fruifly) |
| 290            | (O95840) Thioredoxin-reductase - Homo sapiens (Human)   |
| 291            | (Q9UES8) Thioredoxin-reductase GRIM-12 - Homo sapiens (Human)   |
| 292            | (Q9UH79) Thioredoxin-reductase {GENE:TR} - Homo sapiens (Human)   |
| 293            | (Q9UQU8) Thioredoxin-reductase - Homo sapiens (Human)   |
| 294            | (Q9NNW6) Thioredoxin-reductase TR2 (Fragment) - Homo sapiens (Human)  |
| 295            | (Q9NNW7) Thioredoxin-reductase TR3 - Homo sapiens (Human)   |
| 296            | (Q9P101) Thioredoxin-reductase 3 (Fragment) {GENE:TRXR3} - Homo sapiens (Human)                                 |
| 297            | (Q9P2Y0) Thioredoxin-reductase II beta (EC 1.6.4.5) - Homo sapiens (Human)                                      |
| 298            | (Q9H2Z5) Mitochondrial thioredoxin-reductase {GENE:TRXR2A} - Homo sapiens (Human)                               |
| 299            | (Q99475) KM-102-DERIVED REDUCTASE-LIKE FACTOR (THioredoxin-reductase) - Homo sapiens (Human)                    |
| 300            | (Q99P49) Thioredoxin-reductase 1 {GENE:TXNRD1} - Mus musculus (Mouse)   |
| 301            | (Q9CSV5) Thioredoxin-reductase 1 (Fragment) {GENE:TXNRD1} - Mus musculus (Mouse)                                |
| 302            | (Q9CZE5) Thioredoxin-reductase 1 {GENE:TXNRD1} - Mus musculus (Mouse)   |
| 303            | (Q9JHA7) Thioredoxin-reductase TR3 (GENE:TXNRD2 OR TR3) - Mus musculus (Mouse)                                  |
| 304            | (Q9JLT4) Thioredoxin-reductase {GENE:TXNRD2 OR TRXR2} - Mus musculus (Mouse)                                    |

10

| SEQ. ID<br>NO. | SWISS PROTEIN IDENTIFIER (in parenthesis)  |  |  |
|----------------|--|--|--|
|                | EXAMPLES OF REDOX PROTEINS   |  |  |
| 305            | (Q9JMH5) Thioredoxin-reductase 2 {GENE:TXNRD2 OR TXNRD2} - Mus musculus (Mouse)      |  |  |
| 306            | (Q9JMH6) Thioredoxin-reductase 1 {GENE:TXNRD1 OR TXNRD1} - Mus musculus (Mouse)      |  |  |
| 307            | (O89049) Thioredoxin-reductase - Rattus norvegicus (Rat)                             |  |  |
| 308            | (Q9JKZ3) Thioredoxin-reductase 1 (Fragment) - Rattus norvegicus (Rat)                |  |  |
| 309            | (Q9JKZ4) Thioredoxin-reductase 1 - Rattus norvegicus (Rat)                           |  |  |
| 310            | (Q9JLE6) Thioredoxin-reductase (Fragment) - Rattus norvegicus (Rat)                  |  |  |
| 311            | (Q9R1I3) NADPH-dependent thioredoxin-reductase {GENE:TRR1} - Rattus norvegicus (Rat) |  |  |
| 312            | (Q9Z0J5) Thioredoxin-reductase precursor {GENE:TRXR2} - Rattus norvegicus (Rat)      |  |  |
| 313            | (Q9MYY8) Redox enzyme thioredoxin-reductase - Sus scrofa (Pig)                       |  |  |

## WHAT IS CLAIMED IS:

- A method of producing an oil body associated with a recombinant multimeric-protein-complex, said method comprising:
- (a) producing in a cell comprising oil bodies, a first recombinant polypeptide and 5 a second recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said multimeric-protein-complex; and
  - (b) associating said multimeric-protein-complex with an oil body through an oilbody-targeting-protein capable of associating with said oil body and said first recombinant polypeptide.
  - 2. The method of claim 1 further comprising (c) isolating said oil bodies associated with said recombinant multimeric-protein-complex.
  - The method of claim 1 wherein said multimeric-protein-complex associates with oil bodies obtainable from said cell comprising oil bodies.
- 15 4. The method of claim 1 wherein said multimeric-protein-complex associates intracellularly with said oil bodies.
  - 5. The method of claim 1 wherein said second recombinant polypeptide is associated with a second oil-body-targeting-protein capable of associating with an oil body and said second recombinant polypeptide.
- 20 The method of claim 5 wherein each of said oil-body-targetingproteins is an oil-body-protein or an immunoglobulin.
  - 7. The method of claim 6 wherein said oil-body-targeting-protein is an oleosin or caleosin.
- 8. The method of claim 1 wherein said oil-body-targeting-protein is an oleosin or caleosin and said first recombinant polypeptide is fused to said oleosin 25 or caleosin.
  - 9. The method of claim 8 wherein said second recombinant polypeptide is fused to a second oleosin or second caleosin capable of associating with an oil body.
- 30 10. The method of claim 1 wherein said first and second recombinant polypeptides are produced as a multimeric-fusion-protein comprising said first and second recombinant polypeptide.

PCT/US01/50240

- 11. The method of claim 1, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.
- 12. The method of claim 11 wherein said heteromultimeric-proteincomplex is an enzymatically active redox complex or an immunoglobulin.
- 13. The method of claim 1, wherein said first recombinant polypeptide is 5 capable of associating with said second recombinant polypeptide in the cell.
  - 14. The method of claim 1 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxinreductase.
  - 15. The method of claim 14, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.

10

15

20

25

- 16. The method of claim 14, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
  - 17. The method of claim 1 wherein said cell is a plant cell.
  - 18. The method of claim 1 wherein said cell is a safflower cell.
- 19. The method of claim 1 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
- 20. The method of claim 1 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
- 21. The method of claim 19 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
- 22. A method of expressing a recombinant multimeric-protein-complex comprising a first and second recombinant polypeptide in a cell, said method comprising:
- introducing into a cell a first chimeric nucleic acid sequence comprising: (a)
- (i) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
  - (ii) a second nucleic acid sequence encoding a first recombinant polypeptide;

- (b) introducing into said cell a second chimeric nucleic acid sequence comprising:
- (i) a third nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
- (ii) a fourth nucleic acid sequence encoding a second recombinant 5 polypeptide;
  - (c) growing said cell under conditions to permit expression of said first and second recombinant polypeptide in a progeny cell comprising oil bodies wherein said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimeric-protein-complex; and
- (d) associating said first recombinant polypeptide with an oil body through an oil-body-targeting-protein capable of associating with said oil body and said first recombinant polypeptide.
  - 23. The method of claim 22 further comprising (e) isolating from said progeny cell, oil bodies comprising said multimeric-protein-complex.
- 24. The method of claim 22 wherein said multimeric-protein-complex associates with said oil bodies obtainable from said progeny cell comprising oil bodies.
  - 25. The method of claim 22 wherein said oil bodies associate intracellularly with said multimeric-protein-complex.
- 26. The method of claim 22 wherein said second recombinant polypeptide is associated with a second oil-body-targeting-protein capable of associating with an oil body and said second recombinant polypeptide.
  - 27. The method of claim 26 wherein each of said oil-body-targeting-proteins is selected from an oil-body-protein or an immunoglobulin.
  - 28. The method of claim 27 wherein said oil-body-protein is an oleosin or caleosin.
  - 29. The method of claim 28 wherein said first recombinant polypeptide is fused to said oleosin or caleosin.
- 30. The method of claim 29 wherein said second recombinant polypeptide is fused to a second oleosin or second caleosin capable of associating with an oil body.

15

20

- 31. The method of claim 22 wherein said first and second recombinant polypeptide are produced as a multimeric-fusion-protein comprising said first and second recombinant polypeptide.
- 32. The method of claim 22 wherein said first and second recombinant polypeptide form a multimeric-protein-complex.
  - 33. The method of claim 32, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.
  - 34. The method of claim 32 wherein said heteromultimeric-protein-complex is an enzymatically active redox complex or an immunoglobulin.
- 35. The method of claim 22 wherein said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimericprotein-complex in said progeny cell.
  - 36. The method of claim 22 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
  - 37. The method of claim 36, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
  - 38. The method of claim 36, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
  - 39. The method of claim 22 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
  - 40. The method of claim 22 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
  - 41. The method of claim 39 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
- 30 42. The method of claim 22 wherein said cell is a plant cell.
  - 43. The method of claim 42 wherein said plant cell is a safflower cell.

- 44. A method of producing in a plant a recombinant multimeric-protein-complex, said method comprising:
- (a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide wherein said first recombinant polypeptide is
- capable of associating with said oil bodies through an oil-body-targeting-protein;
  (b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide; and
  - (c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex.
- 45. The method of claim 44 wherein said second recombinant polypeptide is capable of associating with oil bodies through an oil-body-targeting-protein in said second plant.
- 46. The method of claim 44 further comprising (d) isolating from said progeny plant oil bodies comprising said multimeric-protein-complex.
- 47. The method of claim 44 wherein said oil-body-targeting-protein is selected from an oil-body-protein or an immunoglobulin.
- 20 48. The method of claim 47 wherein said oil-body-protein is an oleosin or caleosin.
  - 49. The method of claim 48 wherein said first recombinant polypeptide is fused to said oleosin or caleosin.
- 50. The method of claim 49 wherein said second recombinant polypeptide is fused to a second oleosin or second caleosin capable of associating with an oil body.
  - 51. The method of claim 44 wherein said first and second recombinant polypeptide form a multimeric-protein-complex.
- 52. The method of claim 51, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.
  - 53. The method of claim 52 wherein said heteromultimeric-protein-complex is an enzymatically active redox complex or an immunoglobulin.

- 54. The method of claim 44 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
- 55. The method of claim 54, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
  - 56. The method of claim 54, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 57. The method of claim 44 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
  - 58.. The method of claim 44 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
- 15 59. The method of claim 57 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
  - 60. The method of claim 44 wherein said plant is safflower.
  - 61. A chimeric nucleic acid sequence encoding a multimeric-fusionprotein, said nucleic acid comprising:
- 20 (a) a first nucleic acid sequence encoding an oil-body-targeting-protein operatively linked in reading frame to;
  - (b) a second nucleic acid sequence encoding a first recombinant polypeptide; linked in reading frame to;
- (c) a third nucleic acid sequence encoding a second recombinant polypeptide,
   wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex.
  - 62. The nucleic acid of claim 61, wherein said oil-body-targeting-protein is selected from an oil-body-protein or an immunoglobulin.
- 63. The nucleic acid of claim 62, wherein said oil-body-protein is an oleosin or caleosin.
  - 64. The nucleic acid of claim 63, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.

- 65. The chimeric nucleic acid sequence of claim 61 wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin.
- 66. The chimeric nucleic acid sequence of claim 65 wherein said first and second recombinant polypeptides are a thioredoxin and a thioredoxin-reductase.

5

10

25

- 67. The chimeric nucleic acid of claim 66, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 68. The chimeric nucleic acid of claim 66, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 69. The chimeric nucleic acid of claim 65 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
- 70. The chimeric nucleic acid of claim 65 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
- 71. The chimeric nucleic acid of claim 69 wherein said oil-body targeting-20 protein comprises protein A, protein L or protein G.
  - 72. The nucleic acid of claim 61, wherein positioned between said nucleic acid sequence encoding an oil-body-targeting-protein and said nucleic acid sequence encoding a first recombinant polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.
  - 73. The nucleic acid of claim 72, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
  - 74. The nucleic acid of claim 73, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said sequence encoding the first recombinant polypeptide.

- 75. A recombinant multimeric-fusion-protein comprising (i) an oil-bodytargeting-protein, or fragment thereof, (ii) a first recombinant polypeptide and a (iii) second recombinant polypeptide, wherein said first and second recombinant polypeptides are capable of forming a multimeric-protein-complex.
- 76. The recombinant multimeric-fusion-protein of claim 75 wherein said oil-body-targeting-protein is selected from an oil-body-protein or an immunoglobulin.

15

- 77. The recombinant multimeric-fusion-protein of claim 76 wherein said oil-body-protein is an oleosin or a caleosin.
- 10 78. The recombinant multimeric-fusion-protein of claim 77, wherein said multimeric-fusion-protein is a heteromultimeric-fusion-protein.
  - 79. The recombinant heteromultimeric-fusion-protein of claim 78 wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin.
  - 80. The recombinant fusion polypeptide of claim 79 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
  - 81. The recombinant fusion polypeptide of claim 80, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
  - 82. The recombinant fusion polypeptide of claim 80, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 83. The recombinant fusion polypeptide of claim 75, wherein positioned 25 between said oil-body-targeting-protein and said first recombinant polypeptide is an oil-body-surface-avoiding linker amino acid sequence,
  - 84. The recombinant fusion polypeptide of claim 83, wherein said oilbody-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
- 30 85. The recombinant fusion polypeptide of claim 84, wherein the fusion polypeptide further comprises a linker amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned

WO 02/50289

between the oil-body-surface-avoiding linker amino acid sequence and said first recombinant polypeptide.

- 86. Isolated oil bodies comprising a multimeric-protein-complex comprising (i) an oil-body-targeting-protein and (ii) a first recombinant polypeptide, said oil bodies further comprising a second recombinant polypeptide, wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex.
- 87. Isolated oil bodies of claim 86 wherein said oil-body-targeting-protein is an oil-body-protein or an immunoglobulin.
- 10 88. Isolated oil bodies of claim 87 wherein said oil-body-protein is an oleosin or a caleosin.
  - 89. Isolated oil bodies of claim 88 wherein said first recombinant polypeptide is fused to said oleosin or caleosin.
- 90. Isolated oil bodies of claim 86 wherein said first recombinant polypeptide is fused to said second recombinant polypeptide.
  - 91. The isolated oil bodies of claim 90, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.
  - 92. The isolated oil bodies of claim 91 wherein said heteromultimericprotein-complex is an enzymatically active redox complex or an immunoglobulin.
- 20 93. Isolated oil bodies comprising
  - (a) a first fusion protein comprising a first oil-body-targeting-protein fused to a first recombinant polypeptide; and
  - (b) a second fusion protein comprising a second oil-body-targeting-protein fused to a second recombinant polypeptide,
- wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex.
  - 94. Isolated oil bodies of claim 93 wherein said first oil-body-targetingprotein is an oil-body-protein or an immunoglobulin.
- 95. Isolated oil bodies according claim 93 wherein said first oil-body-30 protein is an oleosin or a caleosin.
  - 96. The isolated oil bodies of claim 93, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.

- 97. Isolated oil bodies of claim 93 wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin.
- 98. Isolated oil bodies of claim 93 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
  - 99. The oil bodies of claim 98, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 100. The oil bodies of claim 98, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
  - 101. The oil bodies of claim 93 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
- 102. The oil bodies of claim 93 wherein said first recombinant15 polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
  - 103. The oil bodies of claim 101 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
- 20 104. A cell comprising oil bodies and (i) an oil-body-targeting-protein, (ii) a first recombinant polypeptide and (iii) a second recombinant polypeptide wherein
  - (1) said first recombinant polypeptide is capable of associating with said oilbody-targeting-protein; and
- 25 (2) said first recombinant polypeptide capable of associating with said second recombinant polypeptide to form a multimeric-protein-complex.
  - 105. The cell of claim 104 wherein said oil-body-targeting-protein is an oil-body-protein or an immunoglobulin.
- 106. The cell of claim 105 wherein said oil-body-protein is an oleosin or caleosin.

- 107. The cell of claim 104 wherein said first recombinant polypeptide is fused to said second recombinant polypeptide so as to form a multimeric-fusion-protein.
- 108. The cell of claim 107 wherein said multimeric-fusion-protein is a heteromultimeric-fusion-protein.
  - 109. The cell of claim 104 wherein said first recombinant polypeptide is fused to said oil-body-targeting-protein.
  - 110. The cell of claim 104 wherein said first recombinant polypeptide is fused to said first oil-body-targeting-protein and said second polypeptide is fused to a second oil-body-targeting-protein.
    - 111. The cell of claim 104 wherein said second recombinant polypeptide is capable of associating with a second oil-body-targeting-protein.
  - 112. The cell of claim 104 wherein said first and second recombinant polypeptide form a heteromultimeric-protein-complex.
- 15 113. The cell of claim 104 wherein said heteromultimeric-protein-complex is an enzymatically active redox complex or an immunoglobulin.

- 114. The cell of claim 104 wherein said first polypeptide is a thioredoxin and said second polypeptide is a thioredoxin-reductase.
- 115. The cell of claim 114, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
  - 116. The cell of claim 114, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 117. The cell of claim 104 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
  - 118. The cell of claim 104 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
- 30 119. The cell of claim 117 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
  - 120. The cell of claim 104 wherein said cell is obtained from a plant.

-135-

- 121. The cell of claim 104 wherein said cell is obtainable from a safflower plant.
  - 122. A plant comprising cells of claim 104.
  - 123. A safflower plant comprising cells of claim 104.
- 124. The method of claim 2 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase, said method further comprising (d) formulating the oil bodies for use in the preparation of a food product, personal care product or pharmaceutical composition.
- 10 125. The method of claim 124, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
  - 126. The method of claim 124, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 15 127. The method of claim 124 wherein said formulating comprises the addition of NADP or NADPH.
  - 128. The method of claim 124 wherein said food product is a milk or wheat based food product.
- 129. The method of claim 124 wherein said personal care product20 reduces the oxidative stress to the surface area of the human body or is used to lighten the skin.
  - 130. The method of claim 124 wherein said pharmaceutical composition is used to treat chronic obstructive pulmonary disease (COPD), cataracts, diabetes, envenomation, bronchiopulmonary disease, malignancies, psoriasis, reperfusion injury, wound healing, sepsis, GI bleeding, intestinal bowel disease (IBD), ulcers, GERD (gastro esophageal reflux disease).
  - 131. A composition comprising isolated oil bodies, thioredoxin and thioredoxin-reductase.

25

132. The composition of claim 131, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.

- 133. The composition of claim 131, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
  - 134. The composition of claim 131 further comprising NADP or NADPH.
- 135. A food product, personal care product or pharmaceutical composition comprising the composition of claim 131.
- 136. The food product, personal care product or pharmaceutical composition of claim 135 further comprising NADP or NADPH.
- 137. The food product of claim 135 wherein said food product is a milk10 based or wheat based food product.
  - 138. The personal care product of claim 135 wherein said personal care product reduces the oxidative stress to the surface area of the human body or is used to lighten the skin.
- 139. The pharmaceutical composition of claim 135 wherein said
  pharmaceutical composition is used to treat chronic obstructive pulmonary disease, cataracts, psoriasis or reperfusion injury.
  - 140. The multimeric-fusion-protein of claim 75, wherein said fusion-protein contains two or more polypeptide chains selected from the group of proteins set forth in Figure 5.
- 20 141. A method of reducing allergenicity of a food comprising the steps of:

providing the isolated oil bodies of claim 78; and adding the isolated oil bodies to the food, whereby allergenicity of the food is reduced.

- 25 142. The method of claim 141, wherein the food is selected from the group consisting of wheat flour, wheat dough, milk, cheese, yogurt and ice cream.
  - 143. The method of claim 141, further comprising providing NADH as a co-factor in the substantial absence of NADPH.
- 30 144. A method of treating or protecting a target against oxidative stress, comprising the steps of:

providing the recombinant fusion polypeptide of claim 46; and

WO 02/50289

contacting the recombinant fusion polypeptide with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress.

- 145. The method of claim 144, wherein the target is selected from the group consisting of a molecule, a molecular complex, a cell, a tissue, and an organ.
  - 146. A method for preparing an enzymatically active redox protein associated with oil bodies comprising:
- a) producing in a cell a redox fusion polypeptide comprising a first
   10 redox protein linked to a second redox protein;
  - b) associating said redox fusion polypeptide with oil bodies through an oil-body-targeting-protein capable of associating with said redox fusion polypeptide and said oil bodies; and
- c) isolating said oil bodies associated with said redox fusion
   polypeptide.
  - 147. The method of claim 146 wherein said oil-body-targeting-protein is an oil-body-protein or an immunoglobulin.
  - 148. The method of claim 146 wherein said oil-body-protein is an oleosin or a caleosin.
- 20 149. The method of claim 146 wherein said first redox protein is a thioredoxin and said second redox protein is a thioredoxin-reductase.
  - 150. The method of claim 149, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 151. The method of claim 149, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
  - 152. The method of claim 146 wherein said cell is a plant cell.
  - 153. The method of claim 146 wherein said cell is a safflower cell.
- 154. A method for preparing a redox protein associated with oil bodies 30 comprising:
  - a) introducing into a cell a chimeric nucleic acid sequence comprising:

-138-

1) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;

- 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
- a third nucleic acid sequence capable of terminating transcription in said cell;
- b) growing said cell under conditions to permit expression of said redox fusion polypeptide in a progeny cell comprising oil bodies; and

5

10

20

- c) isolating from said progeny cell said oil bodies comprising said
   redox fusion polypeptide.
  - 155. The method of claim 154, wherein positioned between said nucleic acid sequence encoding a sufficient portion of an oil-body-protein and said nucleic acid sequence encoding a redox fusion polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.
  - 156. The method of claim 155, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
  - 157. The method of claim 156, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said nucleic acid sequence encoding a redox fusion polypeptide.
  - 158. The method of claim 157, further comprising introducing an enzyme or chemical that cleaves said redox fusion polypeptide from said oil body, thereby obtaining isolated redox fusion polypeptide.
  - 159. The method of claim 154 wherein said oil-body-protein is an oleosin or a caleosin.

- 160. The method of claim 154 wherein said first redox protein is a thioredoxin and said second redox protein is a thioredoxin-reductase.
- 161. The method of claim 160, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 162. The method of claim 160, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
  - 163. The method of claim 154 wherein said cell is a plant cell.
- 164. The method of claim 154 wherein said thioredoxin and thioredoxin-10 reductase is obtained from *Arabidopsis*.
  - 165. The method of claim 146 wherein the first redox protein is at least 5 times more active when produced as a redox fusion polypeptide as compared to the production of the first redox protein without the second redox protein.
    - 166. The method of claim 146 further comprising:
- d) formulating an emulsion of the oil bodies associated with the redox fusion polypeptide for use in the preparation of a product capable of treating oxidative stress in a target, a product capable of chemically reducing a target, pharmaceutical composition, a personal care product or a food product.
  - 167. A chimeric nucleic acid comprising:

5

- 20 1) a first nucleic acid sequence capable of regulating transcription in a host cell operatively linked to;
  - 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
  - a third nucleic acid sequence capable of terminating transcription in said cell.
- 30 168. The chimeric nucleic acid of claim 167 wherein said oil-body-protein is an oleosin or a caleosin.

-140-

- 169. The chimeric nucleic acid of claim 167 wherein said first redox protein is a thioredoxin and said second redox protein is a thioredoxin-reductase.
- 170. The chimeric nucleic acid of claim 169, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 171. The chimeric nucleic acid of claim 169, wherein said thioredoxinreductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.

5

- 172. The chimeric nucleic acid of claim 167 wherein said cell is a plant 10 cell.
  - 173. The chimeric nucleic acid of claim 167, wherein positioned between said nucleic acid sequence encoding a sufficient portion of an oil-body-protein and said nucleic acid sequence encoding a redox fusion polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.
  - 174. The chimeric nucleic acid of claim 173, wherein said oil-bodysurface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
- 175. The chimeric nucleic acid of claim 174, wherein the gene fusion 20 further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said nucleic acid sequence encoding a redox fusion polypeptide.
- 25 176. A transgenenic plant comprising the chimeric nucleic acid sequence of claim 167.
  - 177. The transgenic plant of claim 176, wherein said chimeric nucleic acid is contained within a plastid.
- 178. A safflower plant comprising the chimeric nucleic acid of anyone of claim 167. 30
  - 179. The safflower plant of claim 178, wherein said chimeric nucleic acid is contained within a plastid.

- 180. A plant seed comprising the chimeric nucleic acid of claim 167.
- 181. The plant seed of claim 180, wherein said chimeric nucleic acid is contained within a plastid.
  - 182. A safflower seed comprising the chimeric nucleic acid of claim 168.
- 5 183. The safflower seed of claim 182, wherein said chimeric nucleic acid is contained within a plastid.
  - 184. An oil body preparation obtained by the method of claim 146.
  - 185. A food product comprising an oil body preparation of claim 184.
  - 186. A composition comprising an oil body preparation of claim 184.
- 10 187. A personal care product comprising an oil body preparation of claim 184.
  - 188. A product capable of treating oxidative stress in a target comprising an oil body preparation of claim 184.
- 189. A product capable of chemically reducing a target comprising an oil body preparation of claim 184.
  - 190. A detergent composition comprising the product of claim 184.
  - 191. A method of cleansing an item, comprising administering the product of claim 189 to said item under conditions that promote cleansing.
    - 192. An emulsion formulation prepared by the method of claim 166.
- 20 193. A nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one thioredoxin-related protein or an active fragment thereof.
- 194. The construct of claim 193, wherein the at least one thioredoxinrelated protein is thioredoxin.
  - 195. The construct of claim 194, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 196. The construct of claim 194, wherein the thioredoxin is derived from 30 Arabidopsis or wheat.
  - 197. The construct of claim 193, wherein the at least one thioredoxin-related protein is thioredoxin-reductase.

- 198. The construct of claim 197, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 199. The construct of claim 197, wherein the thioredoxin-reductase is derived from *Arabidopsis* or wheat.
  - 200. The construct of claim 197, wherein the thioredoxin-reductase is an NADPH-dependent thioredoxin-reductase.
  - 201. The construct of claim 193, wherein the second region encodes a thioredoxin and thioredoxin-reductase.
- 10 202. The construct of claim 201, wherein the thioredoxin and thioredoxin-reductase is obtained from *Mycobacterium leprae*.
  - 203. The construct of claim 201, wherein at least one thioredoxin-related protein is an engineered fusion protein.
- 204. The construct of claim 193, wherein the first region precedes, in a 15 5 to 3 direction, the second region.
  - 205. The construct of claim 193, wherein the first region follows, in a 5 ' to 3 ' direction, the second region.
- 206. The construct of claim 193, wherein the gene fusion further comprises a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both.
  - 207. The construct of claim 193, further comprising a seed-specific promoter operably linked to the gene fusion.
- 208. The construct of claim 207, wherein the promoter is a phaseolin promoter.
  - 209. The construct of claim 193, wherein at least one thioredoxinrelated protein is derived from a plant species selected from the group consisting of *Arabidopsis* and wheat.
- 210. The construct of claim 193, wherein at least one thioreoxin-related 30 protein is derived from *E. coli*.

10

15

- 211. The construct of claim 193 further comprising a nucleic acid effective as a termination region in plant cells, operably linked to the gene fusion.
- 212. The construct of claim 193, wherein the gene fusion further comprises a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the linker amino acid sequence is positioned between the first region and the second region.
- 213. The construct of claim 212, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
- 214. The construct of claim 213, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and the second region.
- 215. The construct of claim 193, wherein a region of the gene fusion comprises a plurality of codons, each codon specifying a single amino acid, wherein at least one of the codons is modified from a naturally occurring codon within the region.
- 20 216. The construct of claim 215, wherein the modified codon specifies the same amino acid as the naturally occurring codon, and wherein the modified codon is modified according to a codon preference of a plant.
  - 217. The construct of claim 215, wherein the modified codon specifies an amino acid that is different from the amino acid specified by the naturally occurring codon.
  - 218. A transgenic plant containing a nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof.
- 30 219. The plant of claim 218, wherein the thioredoxin-related protein is thioredoxin.

- 220. The plant of claim 219, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 221. The plant of claim 219, wherein the thioredoxin is derived from *Arabidopsis* or wheat.
- 222. The plant of claim 218, wherein the thioredoxin-related protein is thioredoxin-reductase.

- 223. The plant of claim 222, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 10 224. The plant of claim 222, wherein the thioredoxin-reductase is an NADPH-dependent thioredoxin-reductase.
  - 225. The plant of claim 218, wherein the construct is contained within a plastid.
  - 226. The plant of claim 218, wherein the first thioredoxin-related protein
    is thioredoxin and wherein said construct further comprises a region encoding a thioredoxin-reductase.
    - 227. The plant of claim 226, wherein the thioredoxin and thioredoxin-reductase is obtained from *Mycobacterium leprae*.
- 228. The plant of claim 226, wherein the thioredoxin-related protein is an engineered fusion protein.
  - 229. The plant of claim 218, wherein the first region precedes, in a 5' to 3' direction, the second region.
  - 230. The plant of claim 218, wherein the first region follows, in a 5' to 3' direction, the second region.
- 231. The plant of claim 218, wherein the gene fusion further comprises a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both.
- 232. The plant of claim 218, further comprising a seed-specific promoter30 operably linked to the gene fusion.
  - 233. The plant of claim 232, wherein the promoter is a phaseolin promoter.

15

- 234. The plant of claim 218, wherein the thioredoxin-related protein is derived from a plant species selected from the group consisting of *Arabidopsis* and wheat.
- 235. The plant of claim 218, wherein the thioredoxin-related protein is derived from *E. coli*.
  - 236. The plant of claim 218 further comprising a nucleic acid effective as a termination region in plant cells, operably linked to the gene fusion.
- 237. The plant of claim 218, wherein the gene fusion further comprises a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the nucleic acid encoding the linker amino acid sequence is positioned between the region encoding an oil-body-protein and the region encoding a first thioredoxin-related protein.
  - 238. The plant of claim 237, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
  - 239. The plant of claim 238, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and the region encoding a first thioredoxin-related protein.
  - 240. The plant of claim 218, wherein a region of the gene fusion comprises a plurality of codons, each codon specifying a single amino acid, wherein at least one of the codons is modified from a naturally occurring codon within the region.
- 241. The plant of claim 240, wherein the modified codon specifies the same amino acid as the naturally occurring codon, and wherein the codon is modified according to a codon preference of a plant.
- 242. The plant of claim 240, wherein the modified codon specifies an amino acid that is different from the amino acid specified by the naturally occurring codon.

- 243. The plant of claim 218, wherein the plant is selected from the group consisting of *Arabidopsis* and safflower.
- 244. A transgenic plant comprising a nucleic acid construct a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion
  5 comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, wherein a fusion protein comprising activities of oleosin and the thioredoxin-related protein is produced in a seed of the plant.
- 245. The transgenic plant of claim 244, wherein the plant is selected 10 from the group consisting of *Arabidopsis* and safflower.
  - 246. The transgenic plant of claim 244 wherein the promoter is a phaseolin promoter.
    - 247. The seed of the plant of claim 244.
- 248. The seed of claim 247, comprising a thioredoxin-related protein in a concentration of at least about 0.5% of total cellular seed protein.
  - 249. An extract of the seed of claim 247, wherein the extract comprises an activity of a thioredoxin-related protein.
    - 250. An oil body from the seed of claim 247.
    - 251. Oil produced from the seed of claim 247.
- 252. A method of making a fusion protein comprising a thioredoxinrelated activity, the method comprising the steps of:

providing a transgenic plant comprising a nucleic acid construct comprising a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, the gene fusion encoding a fusion protein comprising a thioredoxin-related activity;

obtaining seeds from the plant; and

recovering the fusion protein by isolating oil bodies from the seeds.

253. The method of claim 252, further comprising the step of fractionating the oil bodies to achieve partial purification of the fusion protein.

25

254. Oil bodies in association with a fusion protein, obtained by the method of claim 252.

5

15

- 255. The method of claim 252 further comprising a step of cleaving the oil-body-protein from the thioredoxin-related protein after fractionation of the oil bodies.
- 256. The method of claim 255, wherein the cleaving step comprises use of a protease.
- 257. The method of claim 255, wherein the cleaving step comprises chemical proteolysis.
- 258. A method of reducing allergenicity of a food comprising the steps of:

providing a preparation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

adding the preparation to the food, whereby allergenicity of the food is reduced due to activity of the thioredoxin-related protein or fragment.

- 259. The method of claim 258, wherein the food is selected from the group consisting of wheat flour, wheat dough, milk, cheese, yogurt and ice cream.
  - 260. The method of claim 258, further comprising providing NADH as a co-factor in the substantial absence of NADPH.
- 261. A composition comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier.
  - 262. The composition of claim 261, further comprising oil bodies in association with the fusion protein.
- 30 263. A cosmetic formulation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active

-148-

fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier.

264. A method of treating or protecting a target against oxidative stress, comprising the steps of:

providing a preparation comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

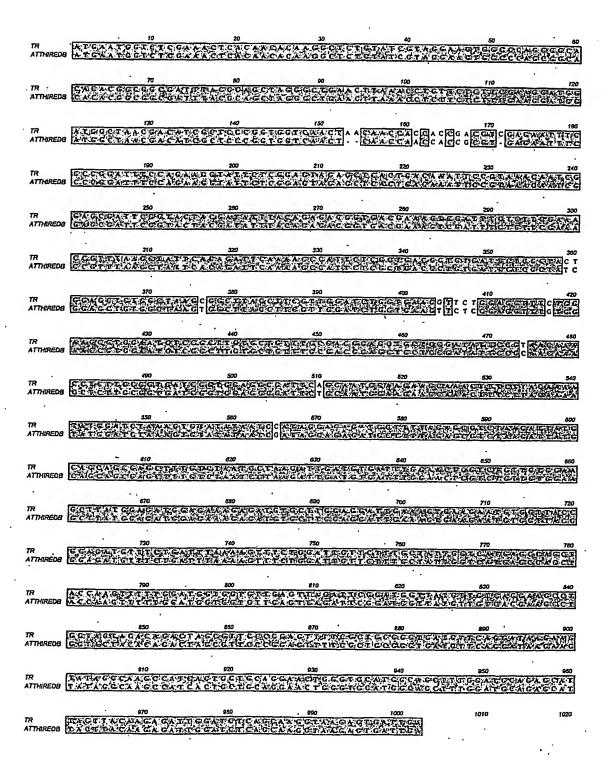
5

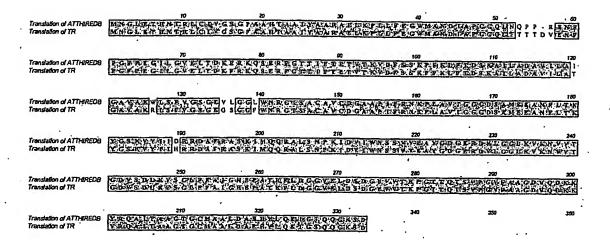
10

contacting the preparation with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress.

265. The method of claim 264, wherein the target is selected from the group consisting of a molecule, a molecular complex, a cell, a tissue, and an organ.

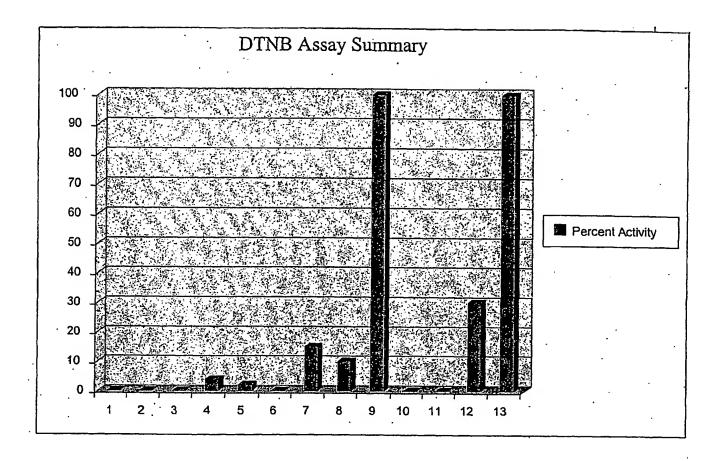
266. A nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one polypeptide or an active fragment thereof, and an oil-body-surface-avoiding linker in frame between the first and second region polypeptides.





| M.lep TR/Trxh<br>Arab TR-link-Trxh   | O DO DESTRUCIO DE LA DESTRUCIO DE LA DELIGIO  |
|--------------------------------------|--|
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | 60 70 80 90 90 100 CO OLITETE DESCRIPTION FRANCISTE FRANCISTE FEETEN KED FEETEN FEETEN KED FEETEN FEETEN KED FEETEN FEETEN KEN DE FEETEN FEETEN FEETEN KEN DE FEETEN FEETE |
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | SEKLEKETES: KYI TYDIXAAN WATEAN AVEREET ARE EER EE 140 EER EER EARLE ARE 120 EER EER EER EER EER EER EER EER EER EE  |
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | 160 170 180 190 200  CAICHGS: PROOD LAKENGALERALERITE ARSWILLERALERALERALERALERITE ARSWILLIAMENTALERALERALERALERALERALERALERALERALERALER   |
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | 210 210 210 210 210 210 210 210 210 210  |
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | 260 170 180 190 100  YMTLGYFFY ANGOMET RESSLYS DYMPTTP PROTYFILL VIRORED STEMP CAY PRACTICAL FLED Q GYESLED SIDIOMANN TIME POINTS Y POWER CONV   |
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | Y DER I VERCOSA PETALAGAS GIO A RAN L'IDECEMM Y IL QE I MOSSICAM ENGINE EN CIDATORE PROPERTI DE TOTAL.  O DER K MERONALI TANA CE TO CEMMAN L'IDECEMM Y IL QE I MOSSICAM ENGINE EN CIDATORE PROPERTI DE TOTAL.  |
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | 160 170 180 190 400 100 100 100 100 100 100 100 100 10   |
| M.lep TR/Trxh -<br>Arab TR-link-Trxh | 410 420 430 430 440 440 450 450 450 450 450 450 450 45   |
| M.lep TR/Trxh<br>Arab TR-link-Trxh   | QGGQPXKELMGAKQKAAARLRDLSQYYPNLN<br>KBEKILLGGAKQKAAARLRDLSQYYPNLN   |

PCT/US01/50240



## HETEROMULTIMERS

| Class          | Heteromultimer  | Example sequence reference for   |
|----------------|---|--|
|                |   | heteromultimeric subunits  |
| Biosynthetic   | 3-methyl-2-oxobutanoate dehydrogenase (2-oxoisovalerate dehydrogenase (lipoamide))— E1 component) | McKean, et al. Biochim. Biophys. Acta (1992)<br>1171:109-112 / Chuang, J.L., et al FEBS Lett. a<br>(1990) 262 (2), 305-309.  |
| Biosynthetic   | 3-oxoadipate CoA-transferase  | Parales, R.E. and Harwood, S.C. J. Bacteriol. (1992) 174:4657-4666   |
| Biosynthetic ' | anthranilate synthase:indole-3-glycerol phosphate synthase  | Zalkin, H.; et al. J. Biol. Chem. (1984) 259:3985-3992.  |
| Biosynthetic   | beta-ketoacyl-[acyl carrier protein] synthase I   | Siggaard-Andersen, M. et al. Proc. Natl. Acad. Sci. U.S.A. (1991) 88:4114-4118   |
| Biosynthetic   | butyrate-acetoacetate CoA-transferase   | Fischer, R.J., et al. J. Bacteriol. (1993) 175, (21), 6959-6969.   |
| Biosynthetic   | cAMP dependent protein kinase   | Mutzel, R et al. Proc. Natl. Acad. Sci. U.S.A. (1987)<br>84:6-10 J Burki, E., et al. Gene (1991) 102 (1), 57-<br>65.   |
| Biosynthetic   | carbamoyl-phosphate synthase  | Shigenobu, S., et al. Nature. (2000) 407 (6800), 81-86.  |
| Biosynthetic   | Creatine kinase   | Billadello, J.J.; et al. Biochem. Biophys. Res. Commun. (1986) 138:392-398. / Roman, D.; et al. Proc. Natl. Acad. Sci. U.S.A. (1985) 82:8394-8398.   |
| Biosynthetic . | gamma-glutamyltransferase (gamma-<br>glutamyl transpeptidase)                                     | Papandrikopoulou, A.; et al. Eur. J. Biochem. (1989) 183:693-698.  |
| Biosynthetic   | glutathione transferase   | Morrow, C.S. et al. Gene (1989) 75:3-11  |
| Biosynthetic   | glycerol-3-phosphate dehydrogenase  | Cole, S.T. et al. J. Bacteriol. (1988) 170:2448-2456.  |
| Biosynthetic   | guanylate cyclase   | Hinsch, K.D. et al. FEBS Lett. (1988) 239:29-34/<br>Koesling, D. et al. FEBS Lett. (1990) 266:128-132.   |
| Biosynthetic   | heterodisulfide reductase   | Smith,D.R., et al. J. Bacteriol. (1997) 179 (22), 7135-7155.   |
| Biosynthetic . | human cathepsin   | Ritonja, A. et al. FEBS Lett. (1988) 228:341-345.  |
| Biosynthetic   | Hydrogenase   | Menon, N.K. et al. J. Bacteriol. (1990) 172:1969-<br>1977.   |
| Biosynthetic   | Meprin A  | Johnson, G.D. and Hersh, L.B. J. Biol. Chem.<br>(1992) 267:13505-13512.  |
| Biosynthetic   | methionine adenosyltransferase  | Horikawa, S.; Tsukada, K. FEBS Lett. (1992)<br>312:37-41.  |
| Biosynthetic   | methylmalonyl-CoA mutase  | Jackson, C.A. et al. Gene (1995) 167:127-132.  |
| Biosynthetic   | mitochondrial processing peptidase  | Pollock, R.A. et al. EMBO J. (1988) 7:3493-3500.   |
| Biosynthetic   | Na+/K+-exchanging ATPase  | Shull, G.E., et al. Biochemistry (1986) 25 (25),<br>8125-8132./Mercer, R.W., et al.<br>Mol. Cell. Biol. (1986) 6 (11), 3884-3890./<br>Mercer, R.W., et al. J. Cell Biol. (1993) 121 (3),<br>579-586. |
| Biosynthetic   | NAD(+)-dependent isocitrate<br>dehydrogenase  | Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem. (1992) 267:16417-16423. /Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem. (1991) 266:22199-22205.   |
| Biosynthetic   | phosphoribosylformylglycinamidine synthase  | Ebbole, D.J.; Zalkin, H. J. Biol. Chem. (1987)<br>262:8274-8287.   |
| Biosynthetic   | protocatechuate 3,4-dioxygenase   | Frazee, R.W.; et al. J. Bacteriol. (1993) 175:6194-6202.   |
| Biosynthetic   | S-100 protein   | Engelkamp, D.; et al. Biochemistry (1992)  |

|                                       | <del></del>                                      | T 01 100 00 100 00 1 1 1 1 1 1 1 1 1 1 1  |
|---------------------------------------|--|---|
|                                       | ·  | 31:10258-10264. / Allore, R.J.; et al. J. Biol. Chem. (1990) 265:15537-15543.   |
| Biosynthetic                          | sucrosefructan 6-fructosyltransferase            | Sprenger, N.; et al. Proc. Natl. Acad. Sci. U.S.A. (1995) 92:11652-11656.   |
| Biosynthetic                          | Superoxide dismutase                             | Capo, C.R.; et al. Biochem. Biophys. Res. Commun. (1990) 173:1186-1193.   |
| Biosynthetic                          | Urease   | Labigne, A.; et al. J. Bacteriol. (1991) 173:1920-1931.   |
| Biosynthetic                          | urokinase-type plasminogen activator (urokinase) | Belin, D. et al. Eur. J. Biochem. (1985) 148:225-232.   |
| Biosythetic                           | methylmalonyl-coenzyme A mutase                  | Birch, A., et al. J. Bacteriol. (1993) 175 (11), 3511-3519.   |
| Calcium binding                       | Calcineurin                                      | Muramatsu, T. and Kincaid, R.L. Biochim. Biophys. Acta (1993) 1178 (1), 117-120 / Guerini, D. et al. DNA (1989) 8:675-682.  |
| Calcium binding                       | Calgranulin                                      | Imamichi, T. et al. Biochem. Biophys. Res.<br>Commun. (1993) 194:819-825.   |
| Calcium binding                       | Calpain  | Aoki, K. et al. FEBS Lett. (1986) 205:313-317.  |
| DNA binding                           | AP1  | van Straaten,F., et al. Proceedings of the National Academy of Sciences of the United States of America. (1983) 80 (11), 3183-3187. /Hattori,K., et al Proceedings of the National Academy of Sciences of the United States of America. (1988) 85 (23), |
|                                       |  | 9148-9152.  |
| DNA binding                           | cMyc-Max   | Schreiber-Agus, N et al. Mol. Cell. Biol. (1993) 13 (5), 2765-2775.   |
| DNA binding                           | DNA binding protein HU-1/HU-2                    | Laine, B. et al. Eur. J. Biochem. (1980) 103:447-461.   |
| DNA binding                           | hepatic nuclear factor 1                         | Bach, I. et al. Nucleic Acids Res. (1992) 20 (16),<br>4199-4204. / Rey-Campos, J. et al. EMBO J. (1991)<br>10 (6), 1445-1457.   |
| DNA binding                           | Integration host factor                          | Miller, H.I. Cold Spring Harbor symposia on<br>quantitative biology. (1984) 49, 691-698. / Flamm,<br>E. and Weisberg, R.A. J. Mol. Biol. (1985) 183:117-<br>128.  |
| DNA binding                           | Ku   | Reeves, W.H. and Sthoeger, Z.M. J. Biol. Chem. (1989) 264 (9), 5047-5052. / J. Biol. Chem. (1989) 264 (23), 13407-13411.  |
| DNA binding                           | MutS   | Bocker et al. 1999. Cancer Research 59, 816-822.  |
| DNA binding                           | NF-E2  | Chan,J.Y. et al Proc. Natl. Acad. Sci. U.S.A. (1993) 90 (23), 11366-11370./ Toki,T., et al. Oncogene (1997) 14 (16), 1901-1910.   |
| DNA binding                           | nuclear factor kB (NFkB)                         | Kieran M, et al. Cell. (1990) Sep 7;62(5):1007-18./<br>Ruben SM, et al. Science (1991) Mar<br>22;251(5000):1490-3.<br>Erratum in: Science (1991) Oct 4;254(5028):11   |
| Electron transport                    | corrinoid/iron-sulfur protein                    | Lu, W.P. et al. J. Biol. Chem. (1993) 268:5605-<br>5614.  |
| Electron transport                    | cytochrome d ubiquinol oxidase                   | Green, G.N. et al. J. Biol. Chem. (1988) 263:13138-13143.   |
| Electron transport                    | cytochrome-c3 hydrogenase                        | Menon, N.K. et al. J. Bacteriol. (1987) 169:5401-5407.  |
| Electron transport                    | electron transfer flavoprotein                   | Finocchiaro, G. et al. Biol. Chem. (1988)<br>263:15773-15780. / Finocchiaro, G. et al. Eur. J.  |
| · · · · · · · · · · · · · · · · · · · | <u> </u>   | Biochem. (1993) 213:1003-1008.  |

| Electron transport | xylene monooxygenase                    | Shaw, J.P. and Harayama, S. Eur. J. Biochem. (1992) 209:51-61. / Kasai, Y., et al. J. Bacteriol.  |
|--------------------|---|---|
|                    |   | (2001) 183 (22), 6662-6666.   |
| Growth factor      | hepatocyte growth factor                | Nakamura, T. et al. Nature (1989) 342:440-443.  |
| Growth factor      | human chorionic gonadotropin            | Morgan, F.J. et al. J. Biol. Chem. (1975) 250 (13), 5247-5258.  |
| Growth factor      | Platelet-derived growth factor          | Takimoto, Y., et al. Hiroshima J. Med. Sci. (1993) 42 (1), 47-52. Josephs, S.F., et al. Science (1984)  |
|                    |   | 225 (4662), 636-639.  |
| Hormone .          | Bombyxin                                | Adachi, T. et al. J. Biol. Chem. (1989) 264:7681- , 7685.   |
| Hormone            | Follicle stimulating hormone            | Fiddes, J.C. and Goodman, H.M. J. Mol. Appl. Genet. (1981) 1 (1), 3-18. / Watkins, P.C., et al. DNA (1987) 6 (3), 205-212.                                      |
| Hormone .          | Insulin                                 | Bell,G.I., Pictet,R.L., Rutter,W.J., Cordell,B.,<br>Tischer,E. and Goodman,H.M.   |
| •                  |   | Sequence of the human insulin gene. Nature. 284 (5751), 26-32 (1980)  |
| Hormone            | Luteinizing Hormone                     | Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.<br>Genet. (1981) 1 (1), 3-18. / Shome, B. and<br>Parlow, A.F. J. Clin. Endocrinol. Metab. (1973) 36                |
| <del></del>        |   | (3), 618-621.   |
| Hormone            | Thyroid stimulating hormone             | Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.<br>Genet. (1981) 1 (1), 3-18. / Hayashizaki Y, et al.<br>FEBS Lett. (1985) 188 (2), 394-400.                       |
| Immune             | B-cell antigen receptor complex         | Hashimoto, S. et al. J. Immunol. (1993) 150 (2), 491-498. / Flaswinkel, H. and Reth, M. Immunogenetics (1992) 36 (4), 266-269.                                  |
| Immune             | Cell surface CD8 molecules              | Ureta-Vidal, A., et al. Immunogenetics (1999) 49 (7-8), 718-721.  |
| Immune             | human complement subcomponent C1q       | Sellar, G.C. et al. Biochem. J. (1991) 274:481-490.   |
| Immune .           | T cell receptor                         | Talken,B.L. et al. Scand. J. Immunol. (2001) 54 (1-2), 204-210.   |
| Photosynthesis -   | C-phycocyanin                           | Offner, G.D. et al. J. Biol. Chem. (1981) 256:12167-12175. / Troxler, R.F. et al. J. Biol. Chem. (1981) 256:12176-12184.  |
| Photosynthesis     | ferroredoxin-thioredoxin reductase      | Chow, L.P. et al. Eur. J. Biochem. (1995) 231:149-<br>156. / Iwadate, H. et al. Eur. J. Biochem. (1994)<br>223:465-471.   |
| Photosynthesis     | Light harvesting complex I              | Proc. Natl. Acad. Sci. U.S.A. (1984) 81, 189-192.   |
| Photosynthetic     | cytochrome b559                         | Carrillo, N. et al. Curr Genet. 1986;10(8):619-24.  |
| Protease           | ATP-dependent Clp protease              | Gerth, U. et al. Gene (1996) 181:77-83. / Kunst,F. et al. Nature (1997) 390 (6657), 249-256.  |
| Receptor           | alpha-2-macroglobulin receptor          | Strickland, D.K. et al. J. Biol. Chem. (1990)<br>265:17401-17404. / Strickland, D.K. et al. J. Biol.<br>Chem. (1991) 266:13364-13369.                           |
| Receptor           | Interleukin-2 receptor                  | Ishida, N. et al. Nucleic Acids Res. (1985) 13:7579-7589. / Hatakeyama, M. et al. Science (1989) 244:551-556 / Takeshita, T. et al. Science (1992) 257:379-382. |
| Receptor           | platelet-derived growth factor receptor | Lee, K.H. et al. Mol. Cell. Biol. (1990) 10:2237-2246. / Herren, B. et al. Biochim. Biophys. Acta 1173 (3), 294-302 (1993).                                     |
| Structural         | Hemoglobin                              | Heindell, H.C. et al. Cell (1978) 15 (1), 43-54.  |

|               |                                      | Best, J.S. et al. Hoppe-Seyler's Z. Physiol. Chem.    |
|---------------|--------------------------------------|---|
|               | 1                                    | (1989) 350 (5), 563-580. / Hardison, R.C. J. Biol.    |
|               |                                      | Chem. (1981) 256 (22), 11780-11786.                   |
| Structural    | human platelet glycoprotein Ib       | Wenger, R.H. et al. Biochem. Biophys. Res.            |
|               |                                      | Commun. (1988) 156 (1), 389-395. / Yagi, M. et al.    |
|               |                                      | J. Biol. Chem. (1994) 269 (26), 17424-17427.          |
| Structural    | Plasma fibronectin                   | Kornblihtt, A.R. et al. Proc. Natl. Acad. Sci. U.S.A. |
|               |                                      | (1983) 80:3218-3222.                                  |
| Structural    | Spectrin                             | Sahr, K.E. et al. J. Biol. Chem. (1990) 265:4434-     |
|               |                                      | 4443. / Winkelmann, J.C. et al. J. Biol. Chem.        |
|               |                                      | (1990) 265:11827-11832.                               |
| Structural    | Tubulin .                            | Ponstingl, H. et al. Proc. Natl. Acad. Sci. U.S.A.    |
|               |                                      | (1981) 78:2757-2761. / Krauhs, E. et al. Proc. Natl.  |
|               |                                      | Acad. Sci. U.S.A. (1981) 78:4156-4160.                |
| Toxin         | Agkisacutacin                        | Cheng, X. et al. Biochem. Biophys. Res. Commun.       |
|               |                                      | (1999) 265 (2), 530-535.                              |
| Toxin         | Beta bungarotoxins                   | Kondo, K. et al. J. Biochem. (1978) 83:101-115.       |
| Toxin         | Crotoxin                             | Bouchier, C. et al. Nucleic Acids Res. (1988) 16      |
|               |                                      | (18), 9050.   |
| Toxin         | Mojave toxin                         | John, T.R. et al. Gene (1994) 139:229-234.            |
| Toxin         | venom protein C9S3                   | Rowan, E.G. et al. Nucleic Acids Res. (1990)          |
|               |                                      | 18:1639. / Joubert, F.J. and Viljoen, C.C. Hoppe-     |
|               |                                      | Seyler's Z. Physiol. Chem. (1979) 360:1075-1090.      |
| Miscellaneous | Inhibin                              | Forage, R.G. et al. Proc. Natl. Acad. Sci. U.S.A.     |
|               |                                      | (1986) 83:3091-3095.                                  |
| Miscellaneous | Monellin                             | Frank, G. and Zuber, H. Hoppe-Seyler's Z. Physiol.    |
| •             |                                      | Chem. (1976) 357:585-592.                             |
| Miscellaneous | mRNA capping enzyme                  | Niles, E.G. et al., J. Virology (1986) 153:96-112.    |
| Miscellaneous | Soybean insulin-binding protein si30 | Barbashov, S.F. et al. Bioorg. Khim. (1991) 17:421-   |
|               |                                      | 423.  |
|               |                                      |   |

## SEQUENCE LISTING

| <110>           | SemBioSys Genetics, Inc.<br>Syngenta Participations AG |           |     |         |
|-----------------|--|-----------|-----|---------|
| <120>           | METHODS FOR THE PRODUCTION OF MULTIMERIC COMPOSITIONS  | PROTEINS, | AND | RELATED |
| <130>           | 38814-351PC  |           |     |         |
|                 |  | •         |     |         |
|                 | Not Yet Assigned<br>Herewith                           |           |     |         |
| <160>           | 313  |           |     |         |
| <170>           | FastSEQ for Windows Version 4.0                        |           |     |         |
| <210>           | 1  |           |     |         |
| <211>           | 22   |           |     |         |
| <212>           | DNA  | •         |     |         |
| <213>           | Artificial Sequence                                    |           |     |         |
| <220>           |  |           |     |         |
| <223>           | Primer   |           |     |         |
| -400-           | 1  |           |     | •       |
| <400><br>taccat | ggct tcggaagaag ga                                     |           |     | 22      |
|                 |  |           |     |         |
| <210>           |  |           |     |         |
| <211>           |  |           |     |         |
| <212>           | DNA  |           |     |         |
| <213>           | Artificial Sequence                                    |           |     |         |
| <220>           |  |           |     |         |
|                 | Primer   |           |     |         |
| -400-           | 2  |           |     | •       |
| <400><br>gaaagc | ttaa gccaagtgtt tg                                     |           |     | 22      |
| 010             | •  |           |     |         |
| <210>           |  |           |     |         |
| <211>           |  |           |     |         |
| <212>           |  |           |     |         |
| <213>           | Artificial Sequence                                    |           |     |         |
| <220>           |  |           |     | ,       |
|                 | Primer   |           |     | ,       |
| <400>           | 3  |           |     |         |
|                 | caca ctaccatgaa tggtctcgaa actcac                      |           |     | 36      |
| •               |  |           |     |         |
| <210>           | 4  |           |     |         |
| <211>           | 28   |           |     |         |
| <212>           | DNA  |           |     |         |
| <213>           | Artificial Sequence                                    |           |     |         |
| <220>           |  |           |     |         |
|                 | Primer   | ,         |     |         |
|                 |  |           |     |         |
| <400>           |  |           |     |         |
| ttaago          | ttca atcactetta cettgetg                               |           |     | 28      |
| <210>           | 5  |           |     |         |
| <211>           | 72   |           |     |         |
| <212>           |  |           |     |         |
|                 | Artificial Sequence                                    |           |     |         |
| <2205           |  |           |     | •       |
| こととける           |  |           |     |         |

```
<223> Primer
actggagatg ttgactcgac ggatactacg gattggtcga cggctatgga agaaggacaa 60
gtgatcgcct gc
<210> 6
<211> 80
<212> DNA
<213> Artificial Sequence
<220>
<223> Primer
<400> 6
atcogtogag toaacatoto cagtttooto ggtggtotog ttagcottog atcoagcaat 60
ctcttgtaag aatgctctgc
<210> 7
<211> 22
<212> DNA
<213> Artificial Sequence
<220>
<223> Primer
<400> 7
                                                                     22
gtggaagett atggagatgg ag
<210> 8
<211> 1002
<212> DNA
<213> Artificial Sequence
<220>
<223> Chimeric
<400> 8
atgaatggtc tcgaaactca caacacaagg ctctgtatcg taggaagtgg cccagcggca 60
atggctaacg acategetee eggtggteaa etaacaacca ceacegaegt egagaattte 180
cccggatttc cagaaggtat tctcggagta gagctcactg acaaattccg taaacaatcg 240
gagegatteg gtactacgat atttacagag acggtgacga aagtegattt ctcttegaaa 300
ccgtttaagc tattcacaga ttcaaaagcc attctcgctg acgctgtgat tctcgctact 360
ggagctgtgg ctaagcggct tagcttcgtt ggatctggtg aaggttctgg aggtttctgg 420
aaccgtggaa totocgottg tgotgtttge gacggagotg otocgatatt cogtaacaaa 480
cctcttgcgg tgatcggtgg aggcgattca gcaatggaag aagcaaactt tcttacaaaa 540 tatggatcta aagtgtatat aatccatagg agagatgctt ttagagcgtc taagattatg 600
cagcagcgag ctttgtctaa tcctaagatt gatgtgattt ggaactcgtc tgttgtggaa 660
gcttatggag atggagaaag agatgtgctt ggaggattga aagtgaagaa tgtggttacc 720 ggagatgttt ctgatttaaa agtttctgga ttgttctttg ctattggtca tgagccagct 780
accaagtttt tggatggtgg tgttgagtta gattcggatg gttatgttgt cacgaagcct 840
ggtactacac agactagcgt tcccggagtt ttcgctgcgg gtgatgttca ggataagaag 900
tataggcaag ccatcactgc tgcaggaact gggtgcatgg cagctttgga tgcagagcat 960
                                                                     1002
tacttacaag agattggatc tcagcaaggt aagagtgatt ga
<210> 9
<211> 999
<212> DNA
<213> Arabidopsis thaliana
atgaatggtc tcgaaactca caacacaagg ctctgtatcg taggaagtgg cccageggca 60
cacaeggegg egatttacge agetaggget gaacttaaac etettetett egaaggatgg 120
atggctaacg acategetec eggtggteaa eteaaceaac cacegegtga gaattteece 180.
ggatttccag aaggtattct cggagtagag ctcactgaca aattccgtaa acaatcggag 240
cgattcggta ctacgatatt tacagagacg gtgacgaaag tcgatttctc ttcgaaaccg 300
```

```
tttaagetat teacagatte aaaagecatt etegetgaeg etgtgattet egetategga 360
getgtggeta agtggettag ettegttgga tetggtgaag tteteggagg tttgtggaac 420
cgtggaatet ccgcttgtgc tgtttgcgac ggagctgctc cgatattccg caacaaacct 480
cttgcggtga tcggtggagg cgattctgca atggaagaag caaactttct tacaaaatat 540
ggatctaaag tgtatataat cgataggaga gatgctttta gagcgtctaa gattatgcag 600
cagogagett tetetaatee taagattgat etgatttega actoetetet tetegaaget 660
tatggagatg gagaaagaga tgtgcttgga ggattgaaag tgaagaatgt ggttaccgga 720
gatgittetg atttaaaagt tietggattg tiettigeta tiggieatga geeagetaee 780 aagtittigg atggiggtgi tigagitagat teggatggit atgtigieae gaageetggi 840
actacacaga ctagcgttcc cggagttttc gctgcgggtg atgttcagga taagaagtat 900
aggcaagcca tcactgctgc aggaactggg tgcatggcag ctttggatgc agagcattac 960
ttacaagaga ttggatctca gcaaggtaag agtgattga
<210> 10
<211> 1002
<212> DNA
<213> Artificial Sequence
<220>
<223> Chimeric
<221> CDS
<222> (1)...(1002)
<223> cDNA encoding NADPH thioredoxin reductase
<400> 10
atg aat ggt ctc gaa act cac aac aca agg ctc tgt atc gta gga agt Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser
                                                                       48
gge eca geg gea cac acg geg geg att tac gea get agg get gaa ett
Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu
aaa cct ctt ctc ttc gaa gga tgg atg gct aac gac atc gct ccc ggt
                                                                       144
Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly
                               40
ggt caa cta aca acc acc gac gtc gag aat ttc ccc gga ttt cca
                                                                       192
Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro
gaa ggt att ctc gga gta gag ctc act gac aaa ttc cgt aaa caa tcg
                                                                       240
Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser
                      70
gag cga ttc ggt act acg ata ttt aca gag acg gtg acg aaa gtc gat
Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp
tto tot tog aaa cog ttt aag ota tto aca gat toa aaa goo att oto
                                                                      336
Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu
             100
get gae get gtg att ete get aet gga get gtg get aag egg ett age
                                                                      384
Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser
ttc gtt gga tct ggt gaa ggt tct gga ggt ttc tgg aac cgt gga atc
                                                                      432
Phe Val Gly Ser Gly Glu Gly Ser Gly Gly Phe Trp Asn Arg Gly Ile
tcc gct tgt gct gtt tgc gac gga gct gct ccg ata ttc cgt aac aaa
                                                                      480
Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys
ect ett geg gtg ate ggt gga gge gat tea gea atg gaa gaa gea aac
                                                                      528
```

| Pro               | Leu        | Ala               | Val               | Ile<br>165 | Gly               | Gly        | Gly               | Asp               | Ser<br>170 | Ala               | Met        | Glu               | Glu               | Ala<br>175 | Asn               |          |
|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|----------|
| ttt<br>Phe        | ctt<br>Leu | aca<br>Thr        | aaa<br>Lys<br>180 | tat<br>Tyr | gga<br>Gly        | tct<br>Ser | aaa<br>Lys        | gtg<br>Val<br>185 | tat<br>Tyr | ata<br>Ile        | atc<br>Ile | cat<br>His        | agg<br>Arg<br>190 | aga<br>Arg | gat<br>Asp        | 576      |
| gct<br>Ala        | ttt<br>Phe | aga<br>Arg<br>195 | gcg<br>Ala        | tct<br>Ser | aag<br>Lys        | att<br>Ile | atg<br>Met<br>200 | cag<br>Gln        | cag<br>Gln | cga<br>Arg        | gct<br>Ala | ttg<br>Leu<br>205 | tct<br>Ser        | aat<br>Asn | cct<br>Pro        | 624      |
|                   |            |                   |                   |            | tgg<br>Trp        |            |                   |                   |            |                   |            |                   |                   |            |                   | 672      |
|                   |            |                   |                   |            | ctt<br>Leu<br>230 |            |                   |                   |            |                   |            |                   |                   |            |                   | 720<br>· |
|                   |            |                   |                   |            | tta<br>Leu        |            |                   |                   |            |                   |            |                   |                   |            |                   | 768 ·    |
|                   |            |                   |                   |            | aag<br>Lys        |            |                   |                   |            |                   |            |                   |                   |            |                   | 816      |
|                   |            |                   |                   |            | acg<br>Thr        |            |                   |                   |            |                   |            |                   |                   |            |                   | 864      |
|                   |            |                   |                   |            | ggt<br>Gly        |            |                   |                   |            |                   |            |                   |                   |            |                   | 912      |
| atc<br>Ile<br>305 | act<br>Thr | gct<br>Ala        | gca<br>Ala        | gga<br>Gly | act<br>Thr<br>310 | gly<br>ggg | tgc<br>Cys        | atg<br>Met        | gca<br>Ala | gct<br>Ala<br>315 | ttg<br>Leu | gat<br>Asp        | gca<br>Ala        | gag<br>Glu | cat<br>His<br>320 | 960      |
|                   |            |                   |                   |            | gga<br>Gly        |            |                   |                   |            |                   |            |                   | tga<br>*          |            |                   | 1002     |

<210> 11 <211> 333

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric

<400> 11

Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser 10 Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly 40 Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro 55 Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser 70 Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp 90 Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu

100 105 110 Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser 120 Phe Val Gly Ser Gly Glu Gly Ser Gly Gly Phe Trp Asn Arg Gly Ile 135 140 Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys 150 155 Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn 165 170 Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg Arg Asp 180 185 Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro 200 Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp 210 215 Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr 230 235 Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly 245 250 His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser 260 265 Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro 280 Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala 295 300 Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His 310 315 Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp 325

<210> 12

<211> 332

<212> PRT

<213> Arabidopsis thaliana

Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser 10 Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu 20 25 Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly 35 40 Gly Gln Leu Asn Gln Pro Pro Arg Glu Asn Phe Pro Gly Phe Pro Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser Glu 70 75 Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp Phe 90 Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu Ala 105 Asp Ala Val Ile Leu Ala Ile Gly Ala Val Ala Lys Trp Leu Ser Phe 115 120 125 Val Gly Ser Gly Glu Val Leu Gly Gly Leu Trp Asn Arg Gly Ile Ser 135 140 Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn, Lys Pro 150 155 Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn Phe 165 170 Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile Asp Arg Arg Asp Ala 180 185 Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro Lys 195 200 205 Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp Gly 215 220 Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr Gly

Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly His 250 245 Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser Asp 265 270 Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro Gly 275 280 Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile 300 295 Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His Tyr 310 315 Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp

<210> 13

<211> 333

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric

<400> 13

Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu 25 Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly 40 35 Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro 55 60 Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser 75 70 Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp 90 Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu 100 105 Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser 115 120 125 Phe Val Gly Ser Gly Glu Gly Ser Gly Gly Phe Trp Asn Arg Gly Ile 135 140 Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys 150 Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn 170 165 Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg Arg Asp 1.90 180 185 Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro 200 205 Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp 215 220 Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr 230 235 Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly 245 250 His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser 265 Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro 280 285 Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala 295 300 Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His 310 315 Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp

```
<210> 14
<211> 3129
<212> DNA
<213> Artificial Sequence
<220>
<221> CDS
<222> (1555) ... (1899)
<223> Chimeric
<400> 14
ctgcaggaat tcattgtact cccagtatca ttatagtgaa agttttggct ctctcgccgg 60
tggtttttta cctctattta aaggggtttt ccacctaaaa attctggtat cattctcact 120 ttacttgtta ctttaatttc tcataatctt tggttgaaat tatcacgctt ccgcacacga 180
tatccctaca aatttattat ttgttaaaca ttttcaaacc gcataaaatt ttatgaagtc 240
ccgtctatct ttaatgtagt ctaacatttt catattgaaa tatataattt acttaatttt 300
agogttggta gaaagcataa tgatttattc ttattcttct tcatataaat gtttaatata 360
caatataaac aaattettta eettaagaag gattteeeat tttatatttt aaaaatatat 420 ttateaaata ttttteaace aegtaaatet eataataata agttgtttea aaagtaataa 480
aatttaactc cataattttt ttattcgact gatcttaaag caacacccag tgacacaact 540
agccattttt ttctttqaat aaaaaaatcc aattatcatt gtatttttt tatacaatga 600
aaatttcacc aaacaatcat ttgtggtatt tctgaagcaa gtcatgttat gcaaaattct 660
ataattccca tttgacacta cggaagtaac tgaagatctg cttttacatg cgagacacat 720
cttctaaagt aattttaata atagttacta tattcaagat ttcatatatc aaatactcaa 780
tattacttct aaaaaattaa ttagatataa ttaaaatatt acttttttaa ttttaagttt 840
aattgttgaa tttgtgacta ttgatttatt attctactat gtttaaattg ttttatagat 900
agtttaaagt aaatataagt aatgtagtag agtgttagag tgttacccta aaccataaac 960
tataagattt atggtggact aattttcata tatttcttat tgcttttacc ttttcttggt 1020
atgtaagtcc gtaactggaa ttactgtggg ttgccatggc actctgtggt cttttggttc 1080
atgcatggat gcttgcgcaa gaaaaagaca aagaacaaag aaaaaagaca aaacagagag 1140
acaaaacgca atcacacaac caactcaaat tagtcactgg ctgatcaaga tcgccgcgtc 1200
catgtatgtc taaatgccat gcaaagcaac acgtgcttaa catgcactit aaatggctca 1260
cccatctcaa cccacacaca aacacattgc ctttttcttc atcatcacca caaccacctg 1320
tatatattca ttctcttccg ccacctcaat ttcttcactt caacacacgt caacctgcat 1380
atgcgtgtca tcccatgccc aaatctccat gcatgttcca accaccttct ctcttatata 1440
1
gct tcg gaa gaa gga caa gtg atc gcc tgc cac acc gtt gag aca tgg
Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr Trp
                                                                      1605
                                                                      1653
aac gag cag ctt cag aag gct aat gaa tcc aaa act ctt gtg gtg gtt
Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val Val
gat ttc acg gct tct tgg tgt gga cca tgt cgt ttc atc gct cca ttc
                                                                      1701
Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro Phe
ttt gct gat ttg gct aag aaa ctt cct aac gtg ctt ttc ctc aag gtt
                                                                      1749
Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val Leu Phe Leu Lys Val
                                                                      1797
gat act gat gaa ttg aag tcg gtg gca agt gat tgg gcg ata cag gcg
Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln Ala
atg cca acc ttc atg ttt ttg aag gaa ggg aag att ttg gac aaa gtt
                                                                      1845
Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys Val
gtt gga gcc aag aaa gat gag ctt cag tct acc att gcc aaa cac ttg
                                                                      1893
Val Cly Ala Lys Lys Asp Clu Leu Gln Ser Thr Ile Ala Lys His Leu
```

PCT/US01/50240 WO 02/50289

110

105

gct taa gcttaataag tatgaactaa aatgcatgta ggtgtaagag ctcatggaga 1949

```
gcatggaata ttgtatccga ccatgtaaca gtataataac tgagctccat ctcacttctt 2009 ctatgaataa acaaaggatg ttatgatata ttaacactct atctatgcac cttattgttc 2069 tatgataaat ttcctcttat tattataaat catctgaatc gtgacggctt atggaatgct 2129
tcaaatagta caaaaacaaa tgtgtactat aagactttct aaacaattct aactttagca 2189
ttgtgaacga gacataagtg ttaagaagac ataacaatta taatggaaga agtttgtctc 2249
gttgatatgt atatgaaagg gtactatttg aactctctta ctctgtataa aggttggatc 2489
atccttaaag tgggtctatt taattttatt gcttcttaca gataaaaaaa aaattatgag 2549
tatgtatata aatttattat aatataacat ttatctataa aaaagtaaat attgtcataa 2669
atctatacaa tcgtttagcc ttgctggacg actctcaatt atttaaacga gagtaaacat 2729 atttgacttt ttggttattt aacaaattat tatttaacac tatatgaaat ttttttttt 2789
tatoggcaag gaaataaaat taaattagga gggacaatgg tgtgtcccaa tccttataca 2849
accaacttcc acaggaaggt caggtcgggg acaacaaaaa aacaggcaag ggaaattttt 2909
taatttgggt tgtcttgttt gctgcataat ttatgcagta aaacactaca cataaccctt 2969
caaagaataa ataaaataaa atgagacact tcagggatgt ttcaaccctt atacaaaacc 3089
ccaaaaacaa gtttcctagc accctaccaa ctaaggtacc
```

<210> 15

<211> 114

<212> PRT

<213> Artificial Sequence

100

<220>

<223> Chimeric

<400> 15

Met Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr 1 5 10 Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val 20 25 Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val Leu Phe Leu Lys 55 Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln 7.0 75 Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys 90 Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr Ile Ala Lys His

Leu Ala

<210> 16

<211> 3888

<212> DNA

<213> Artifcial sequence

<220>

<223> Chimeric

<221> CDS

<222> (1555) ... (1907)

<221> CDS

<222> (2148)...(2659)

| tratte against the tratter against the tra | agggetttt<br>ttggteta<br>ataa<br>atte<br>ttaa<br>atte<br>ttaa<br>actt<br>agat<br>agag<br>atggteta<br>tate<br>ttaa<br>agag<br>taggteta | aat<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>ttaa<br>t | cctccataaattaattaattaattaattaattaattaat | tatt<br>tattt<br>tattt<br>tattt<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tcatta<br>tca | ttagatctaattaatgcaaaacccaattaattaatgcaataattaat | agggggcata<br>teatta<br>teatta<br>gctta<br>teatta<br>teatta<br>ggat<br>teatta<br>teatta<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accacaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accacaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accacaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accacaca<br>accaca<br>accacaca<br>accacaca<br>accaca<br>accaca<br>accaca<br>accacaca<br>accacaca<br>accaca<br>accacaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accaca<br>accacaca<br>accaca<br>accaca<br>accacaca<br>accaca<br>accacaca<br>accacaca<br>accacacaca<br>accacaca<br>accacacaca<br>accacacacaca<br>accacacacacacacacacacacacacacacacacacaca | gttt<br>atct<br>atattt<br>aatttt<br>aacgatcc<br>agttatt<br>tttat<br>ggatatt<br>tttat<br>ggataa<br>ggttatt<br>tttat<br>ggataa<br>ggttatt<br>tttat<br>ggataa<br>ggttatt<br>tttat<br>gataa<br>ggttatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>tttat<br>gatatt<br>gatatt<br>tttat<br>gatatt<br>gatatt<br>tttat<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>gatatt<br>g | ttatogitotoaat gagatoottoto | acctgattattattattattattattattattattattattat | aaaatcaataagtaatcaatcaatcaataagttaagtaataagtaataagtaag | attation of the state of the st | ctgggaaaaatattcttacttacttacttacttacttact | toatattoattattoagaattogcatttttttattattattattattattattattattatta | catt<br>cattactt<br>acttaa<br>gaaattaa<br>gcaaatttacttaa<br>ttaa | cycacyctta<br>gaattataacaattcaa<br>acaattcaa<br>acaattcaa<br>acaattcaa<br>acaattcaa<br>acaattcy<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaagca<br>acaattcy<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaagctty<br>acaaaaagctty<br>acaaaaagctty<br>acaaaaagctty<br>acaaaaaaagctty<br>acaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa | 120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>660<br>720<br>780<br>840<br>960<br>1020<br>1140<br>1260<br>1320<br>1380<br>1440 |
|--|---|--|---|--|---|---|---|-----------------------------|---|--|--|--|---|--|--|---|
|  |   |  |   |  |   |   |   |                             |   |  |  |  |   | gac<br>Asp   |  | 1605  |
| tac<br>Tyr   | ccg<br>Pro  | atg<br>Met<br>20   | atg<br>Met                              | ggc<br>Gly   | cga<br>Arg                                      | gac<br>Asp  | cga<br>Arg<br>25  | gac<br>Asp                  | cag<br>Gln                                  | tac<br>Tyr   | cag<br>Gln   | atg<br>Met<br>30                         | tcc<br>Ser  | gga<br>Gly   | cga<br>Arg   | 1653  |
|  |   |  |   |  |   |   |   |                             |   |  |  |  |   | act<br>Thr   |  | 1701  |
| gtc<br>Val<br>50   | aca<br>Thr  | gct<br>Ala   | ggt<br>Gly                              | ggt<br>Gly   | tcc<br>Ser<br>55                                | ctc<br>Leu  | ctt<br>Leu  | gtt<br>Val                  | ctc<br>Leu                                  | tcc<br>Ser<br>60                                       | agc<br>Ser   | ctt<br>Leu                               | acc<br>Thr  | ctt<br>Leu   | gtt<br>Val<br>65   | 1749  |
| gga<br>Gly   | act<br>Thr  | gtc<br>Val   | ata<br>Ile                              | gct<br>Ala<br>70   | ttg<br>Leu                                      | act<br>Thr  | gtt<br>Val  | gca<br>Ala                  | aca<br>Thr<br>75                            | cct<br>Pro   | ctg<br>Leu   | ctc<br>Leu                               | gtt<br>Val  | atc<br>Ile<br>80   | ttc<br>Phe   | 1797  |
|  |   |  |   |  |   |   |   |                             |   |  |  |  |   | atc<br>Ile   |  | 1845  |
| ggt<br>Gly   | ttt<br>Phe  | ctt<br>Leu<br>100  | tcc<br>Ser                              | tct<br>Ser   | gga<br>Gly                                      | gly<br>aaa  | ttt<br>Phe<br>105   | ggc<br>Gly                  | att<br>Ile                                  | gcc<br>Ala   | gct<br>Ala   | ata<br>Ile<br>110                        | acc<br>Thr,   | gtt<br>Val   | ttc<br>Phe   | 1893  |
| Ser  |   |  |   |  | gtaag   | gcaca   | ac at   | ttat                        | cato  | : tta  | ctto   | cata                                     | att   | ttgtg  | ıca  | 1947  |
| atatgtgcat gcatgtgttg agccagtagc tttggatcaa tttttttggt cgaataacaa 2 atgtaacaat aagaaattgc aaattctagg gaacatttgg ttaactaaat acgaaatttg 2 acctagctag cttgaatgtg tctgtgtata tcatctatat aggtaaaatg cttggtatga 2 tacctattga ttgtgaatag g tac gca acg gga gag cac cca cag gga tca  Tyr Ala Thr Gly Glu His Pro Gln Gly Ser   |   |  |   |  |   |   |   |                             |   |  |  | 2067                                     |   |  |  |   |

125 120

| gac<br>Asp  | aag<br>Lys<br>130 | ttg<br>Leu | gac<br>Asp        | agt<br>Ser        | gca<br>Ala | agg<br>Arg<br>135 | atg<br>Met | aag<br>Lys        | ttg<br>Leu        | gga<br>Gly | agc<br>Ser<br>140 | aaa<br>Lys | gct<br>Ala   | cag<br>Gln        | gat<br>Asp | 2226 |
|---|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|--|-------------------|------------|------|
|   |                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            |  | ggg               |            | 2274 |
|   |                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            |  | gct<br>Ala<br>175 |            | 2322 |
| gaa<br>Glu  | gaa<br>Glu        | gga<br>Gly | caa<br>Gln<br>180 | gtg<br>Val        | atc<br>Ile | gcc<br>Ala        | tgc<br>Cys | cac<br>His<br>185 | acc<br>Thr        | gtt<br>Val | gag<br>Glu        | aca<br>Thr | tgg<br>Trp<br>190  | aac<br>Asn        | gag<br>Glu | 2370 |
|   |                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            |  | gat<br>Asp        |            | 2418 |
| acg<br>Thr  | gct<br>Ala<br>210 | tct<br>Ser | tgg<br>Trp        | tgt<br>Cys        | gga<br>Gly | cca<br>Pro<br>215 | tgt<br>Cys | cgt<br>Arg        | ttc<br>Phe        | atc<br>Ile | gct<br>Ala<br>220 | cca<br>Pro | ttc<br>Phe   | ttt<br>Phe        | gct<br>Ala | 2466 |
|   |                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            |  | gat<br>Asp        |            | 2514 |
| gat<br>Asp  | gaa<br>Glu        | ttg<br>Leu | aag<br>Lys        | tcg<br>Ser<br>245 | gtg<br>Val | gca<br>Ala        | agt<br>Ser | gat<br>Asp        | tgg<br>Trp<br>250 | gcg<br>Ala | ata<br>Ile        | cag<br>Gln | gcg<br>Ala   | atg<br>Met<br>255 | cca<br>Pro | 2562 |
|   |                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            |  | gtt<br>Val        |            | 2610 |
|   |                   |            |                   |                   | ctt<br>Leu |                   |            |                   |                   |            |                   |            |  | gct<br>Ala        | taa<br>*   | 2658 |
| catggaatat tgtatccgac catgtaacag tataataact gagctccatc tcacttcttc 276 tatgaataaa caaaggatgt tatgatatat taacactcta tctatgcacc ttattgttct 282 atgataaatt tcctcttatt attataaatc atctgaatcg tgacggctta tggaatgct 286 caaatagtac aaaaacaaat gtgtactata agactttcta aacaattcta actttagcat 294 tgtgaacgag acataagtgt tatgatatat aacaattat aatggaagaa gtttgtctcc 306 attataaaga gagaagtttg tatccattta tatatattac acttatata actaccatt tatatattat 312 acttatccac ttatttaatg tctttataag gtttgatcca tggtatttct aatatttata 318 tcgatatgta tatgaaaggg tatattttga acttcttacac tctgatataa gggttgatca 324 tccttaaagt gggtctattt attatattg cttcttacac ataaaaaaa aattatgagt tggtttgata aatttatata atataacat tatcataaa taataaata |                   |            |                   |                   |            |                   |            |                   |                   |            |                   |            | 2829<br>2889<br>2949<br>3009<br>3129<br>3189<br>3369<br>3369<br>3489<br>3549<br>3669<br>3729<br>3789 |                   |            |      |

<210> 17 <211> 118 <212> PRT

## <213> Artifcial sequence

<400> 17 Met Ala Asp Thr Ala Arg Gly Thr His His Asp Ile Ile Gly Arg Asp 10 Gln Tyr Pro Met Met Gly Arg Asp Arg Asp Gln Tyr Gln Met Ser Gly 25 Arg Gly Ser Asp Tyr Ser Lys Ser Arg Gln Ile Ala Lys Ala Ala Thr 40 Ala Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu Val Gly Thr Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu Val Ile 75 Phe Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile 90 Thr Gly Phe Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile Thr Val 100 Phe Ser Trp Ile Tyr Lys 115

<210> 18 <211> 169 <212> PRT <213> Artifcial sequence

<400> 18 Tyr Ala Thr Gly Glu His Pro Gln Gly Ser Asp Lys Leu Asp Ser Ala 10 Arg Met Lys Leu Gly Ser Lys Ala Gln Asp Leu Lys Asp Arg Ala Gln Tyr Tyr Gly Gln Gln His Thr Gly Gly Glu His Asp Arg Asp Arg Thr 40 Arg Gly Gln His Thr Thr Met Ala Ser Glu Glu Gly Gln Val Ile 55 Ala Cys His Thr Val Glu Thr Trp Asn Glu Gln Leu Gln Lys Ala Asn 70 Glu Ser Lys Thr Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly 90 Pro Cys Arg Phe Ile Ala Pro Phe Phe Ala Asp Leu Ala Lys Lys Leu 100 105 110 Pro Asn Val Leu Phe Leu Lys Val Asp Thr Asp Glu Leu Lys Ser Val 120 Ala Ser Asp Trp Ala Ile Gln Ala Met Pro Thr Phe Met Phe Leu Lys 135 140 Glu Gly Lys Ile Leu Asp Lys Val Val Gly Ala Lys Lys Asp Glu Leu 150 Gln Ser Thr Ile Ala Lys His Leu Ala 165

<210> 19
<211> 3888
<212> DNA
<213> Artificial Sequence
<220>
<223> Chimeric
...
<221> CDS
<222> (1555)...(2249)
<221> CDS
<222> (2490)...(2658)
<400> 19
ctgcaggaat tcattgtact coca

| ttattagcaaaattattagcaaaattattaattaattaat | ctctattataaattccattataaagggattatattattattaatta | taatacactacatgattcaactaccactacattcattcat | ctttaattaattaattaattaattaattaattaattaat | aatttattattattattattattattattattattatta | tagatotaattaatgcaaaaccca<br>ttotoatattaaattaactagca<br>ttotoatattaattgcaat | cata cata tgatt taatt gatta taatt aagta taaagt taaact taaact aaacaacc aacacc aatca | atct<br>aaattt<br>aatttaac<br>aagatct<br>aagatcac<br>gtacta<br>ttataac<br>gacaaa<br>gattatt<br>acgacaa<br>gattatt<br>acgacaa<br>gattatt<br>accgacaa<br>gattatt<br>accgacaa<br>accaa<br>caattt<br>accaa<br>caattt<br>accaa<br>caattt<br>accaa<br>caattt<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>caattat<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>accaa<br>acca<br>accaa<br>accaa<br>acca<br>acca<br>acca<br>acca<br>acca<br>acca<br>acca<br>acca<br>acca<br>ac<br>ac | t at c gt t c t c a a t g a g a t c c t t c t c t a a t t a t t a c t t c t | gttattcatttattaagaaaattcatcatttattaagaaaattcatttattt | aaacaataagtaaatcaatcaataagtaagtaagtaagta | tactacttacttactacctacctacctacctacctacct | cacg<br>taaaa<br>tatatat<br>cattgc<br>tattattattattaacat<br>tattaacat<br>gatcacacacacacacacacacacacacacacacacacac | cattattattagttattattattattattattattattatt | ccgctatttacttaaaccaacttttcaacctaaaccaacc | ctcact acacga gaattta gaattatatacacacttacacacttacacacttcacacttcacactcacactcaccac | 180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>780<br>900<br>960<br>1080<br>1140<br>1260<br>1320<br>1380<br>1440 |
|--|--|--|---|---|--|--|--|---|--|--|---|---|---|--|--|---|
| gct<br>Ala                               | tcg<br>Ser                                     | gaa<br>Glu                               | gaa<br>Glu<br>5                         | gga<br>Gly                              | caa<br>Gln   | gtg<br>Val   | atc<br>Ile   | gcc<br>Ala<br>10  | tgc<br>Cys   | cac<br>His                               | acc<br>Thr                              | gtt<br>Val  | gag<br>Glu<br>15                          | aca<br>Thr                               | tgg<br>Trp   | 1605  |
| aac<br>Asn                               | gag<br>Glu                                     | cag<br>Gln<br>20                         | ctt<br>Leu                              | cag<br>Gln                              | aag<br>Lys   | gct<br>Ala   | aat<br>Asn<br>25   | gaa<br>Glu  | tcc<br>Ser   | aaa<br>Lys                               | act<br>Thr                              | ctt<br>Leu<br>30  | gtg<br>Val                                | gtg<br>Val                               | gtt<br>Val   | 1653  |
|  |  |  |   |   |  |  |  |   |  |  |   |   |   | cca<br>Pro                               |  | 1701  |
|  |  |  |   |   |  |  |  |   |  |  |   |   |   | aag<br>Lys                               |  | 1749  |
| gat<br>Asp                               | act<br>Thr                                     | gat<br>Asp                               | gaa<br>Glu                              | ttg<br>Leu<br>70                        | aag<br>Lys   | tcg<br>Ser   | gtg<br>Val   | gca<br>Ala  | agt<br>Ser<br>75                                     | gat<br>Asp                               | tgg<br>Trp                              | gcg<br>Ala  | ata<br>Ile                                | cag<br>Gln<br>80                         | gcg<br>Ala   | 1797  |
|  |  |  |   |   |  |  |  |   |  |  |   |   |   | aaa<br>Lys                               |  | 1845  |
|  |  |  |   |   |  |  |  |   |  |  |   |   |   | cac<br>His                               |  | 1893  |
| gct<br>Ala                               | atg<br>Met<br>115                              | gcg<br>Ala                               | gat<br>Asp                              | aca<br>Thr                              | gct<br>Ala   | aga<br>Arg<br>120  | gga<br>Gly   | acc<br>Thr  | cat<br>His   | cac<br>His                               | gat<br>Asp<br>125                       | atc<br>Ile  | atc<br>Ile                                | ggc<br>Gly                               | aga<br>Arg   | 1941  |
| gac<br>Asp<br>130                        | cag<br>Gln                                     | tac<br>Tyr                               | ccg<br>Pro                              | atg<br>Met                              | atg<br>Met<br>135  | ggc<br>Gly   | cga<br>Arg   | gac<br>Asp  | cga<br>Arg   | gac<br>Asp<br>140                        | cag<br>Gln                              | tac<br>Tyr  | cag<br>Gln                                | atg<br>Met                               | tcc<br>Ser<br>145  | 1989  |
|  |  |  |   |   |  |  |  |   |  |  |   |   |   | gct<br>Ala<br>160                        |  | 2037  |

<210> 20 <211> 232

```
<212> PRT
<213> Artificial Sequence
<220>
<223> Chimeric
<400> 20
Met Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr
                                    10
Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val
          20
                                25
Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro
                            40
Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val Leu Phe Leu Lys
                        55
Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln
                    70
Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys
                                    90
Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr Ile Ala Lys His
                                105
Leu Ala Met Ala Asp Thr Ala Arg Gly Thr His His Asp Ile Ile Gly
                            120
Arg Asp Gln Tyr Pro Met Met Gly Arg Asp Arg Asp Gln Tyr Gln Met
                        135
                                            140
Ser Gly Arg Gly Ser Asp Tyr Ser Lys Ser Arg Gln Ile Ala Lys Ala
                    150
                                        155
Ala Thr Ala Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu
                165
                                    170
                                                        175
Thr Leu Val Gly Thr Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu
           180
                                185
                                                    190
Val Ile Phe Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu
                            200
Leu Ile Thr Gly Phe Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile
                        215
Thr Val Phe Ser Trp Ile Tyr Lys
                    230
<210> 21
<211> 55
<212> PRT
<213> Artificial Sequence
<220>
<223> Chimeric
<400> 21
Tyr Ala Thr Gly Glu His Pro Gln Gly Ser Asp Lys Leu Asp Ser Ala
Arg Met Lys Leu Gly Ser Lys Ala Gln Asp Leu Lys Asp Arg Ala Gln
                                25
Tyr Tyr Gly Gln Gln His Thr Gly Glu His Asp Arg Asp Arg Thr
      35
Arg Gly Gly Gln His Thr Thr
   50
<210> 22
<211> 3787
<212> DNA
<213> Artificial Sequence
<220>
<223> Chimeric
<221> CDS
```

<222> (1555)...(2556)

| traction against the state of t | tttt<br>cttgl<br>cctal<br>cctal<br>cctal<br>cctal<br>cttal<br>cttal<br>cttal<br>cttal<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cattl<br>cat | atta catta c | cctciccatatatatatatatatatatatatatatatata | tatttaattaatataataataataataataataataata | ta de te de | agggggcata<br>tgatta<br>tgatta<br>tgatta<br>tgaga<br>tagga<br>tagga<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>tagat<br>ta<br>ta<br>ta<br>ta<br>ta<br>ta<br>ta<br>ta<br>ta<br>ta<br>ta<br>ta<br>t | gttti<br>atcti<br>atatti<br>atatti<br>atagatci<br>atatti<br>atatti<br>atcatti<br>atcata<br>ggataati<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atcata<br>atca<br>atca<br>atca<br>atca<br>atca<br>atca<br>atca<br>atca<br>atca<br>a<br>atca<br>a<br>atca<br>a<br>a<br>a | t ta control to the c | accti<br>gttga<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>acctt<br>ttata<br>ttata<br>ttattca<br>ttata<br>ttattca<br>ttata<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattca<br>ttattatta<br>ttatta<br>ttatta<br>ttatta<br>ttatta<br>ttatta | aaaa<br>aaaatcaaaatcaaatcaaatcaaatcaaatcaa | tate grant to the transfer of | ctgg<br>cacg<br>taaaa<br>tatat<br>tatat<br>tattt<br>tattt<br>taact<br>tatat<br>taaca<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaac<br>tattaa<br>tattaa<br>tattaa<br>tattaa<br>tattaa<br>tattaa<br>tattaa<br>tattaa<br>tatt | to a tract a tract to a grant to a tract to a grant to a tract a trac | catte catte catte actta acta acta acta a | cgccgg<br>ctcacga<br>gaattta<br>acaattta<br>acaattata<br>acaattcata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattatata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattatata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata<br>acattata | 120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>660<br>720<br>840<br>900<br>1020<br>1140<br>1260<br>1320<br>1380<br>1440 |
|--|--|--|--|---|---|--|--|--|--|--|---|---|--|--|---|--|
|  |  |  |  |   |   |  |  |  |  |  |   |   |  | agt<br>Ser                               |   | 1605   |
| cca<br>Pro   | gcg<br>Ala   | gca<br>Ala<br>20   | cac<br>His                               | acg<br>Thr                              | gcg<br>Ala  | gcg<br>Ala   | att<br>Ile<br>25   | tac<br>Tyr   | gca<br>Ala   | gct<br>Ala                                 | agg<br>Arg  | gct<br>Ala<br>30  | gaa<br>Glu   | ctt<br>Leu                               | aaa<br>Lys  | 1653   |
| cct<br>Pro   | ctt<br>Leu<br>35   | ctc<br>Leu   | ttc<br>Phe                               | gaa<br>Glu                              | gga<br>Gly  | tgg<br>Trp<br>40   | atg<br>Met   | gct<br>Ala   | aac<br>Asn   | gac<br>Asp                                 | atc<br>Ile<br>45  | gct<br>Ala  | ccc<br>Pro   | ggt<br>Gly                               | ggt<br>Gly  | 1701   |
| caa<br>Gln<br>50   | cta<br>Leu   | aca<br>Thr   | acc<br>Thr                               | acc<br>Thr                              | acc<br>Thr<br>55  | gac<br>Asp   | gtc<br>Val   | gag<br>Glu   | aat<br>Asn   | ttc<br>Phe<br>60                           | ccc<br>Pro  | gga<br>Gly  | ttt<br>Phe   | cca<br>Pro                               | gaa<br>Glu<br>65  | 1749   |
| ggt<br>Gly   | att<br>Ile   | ctc<br>Leu   | gga<br>Gly                               | gta<br>Val<br>70                        | gag<br>Glu  | ctc<br>Leu   | act<br>Thr   | gac<br>Asp   | aaa<br>Lys<br>75   | ttc<br>Phe                                 | cgt<br>Arg  | aaa<br>Lys  | caa<br>Gln   | tcg<br>Ser<br>80                         | gag<br>Glu  | 1797   |
|  |  |  |  |   |   |  |  |  |  |  |   |   |  | gat<br>Asp                               |   | 1845   |
|  |  |  |  |   |   |  |  |  |  |  |   |   |  | ctc<br>Leu                               |   | 1893   |
| gac<br>Asp   | gct<br>Ala<br>115  | gtg<br>Val   | att<br>Ile                               | ctc<br>Leu                              | gct<br>Ala  | act<br>Thr<br>120  | gga<br>Gly   | gct<br>Ala   | gtg<br>Val   | gct<br>Ala                                 | aag<br>Lys<br>125   | cgg<br>Arg  | ctt<br>Leu   | agc<br>Ser                               | ttc<br>Phe  | 1941   |
|  |  |  |  |   |   |  |  |  |  |  |   |   |  | atc<br>Ile                               |   | 1989   |
|  |  |  |  |   |   |  |  |  |  |  |   |   |  |  |   |  |

| gct tgt gct gtt<br>Ala Cys Ala Va   | tgc gac gga<br>Cys Asp Gly<br>150   | a gct gct ccg at<br>/ Ala Ala Pro Il<br>155 | a ttc cgt aac aa<br>e Phe Arg Asn Ly<br>16  | s Pro                      |  |  |  |  |  |
|---|-------------------------------------|---|---|----------------------------|--|--|--|--|--|
|   | e Gly Gly Gly                       |   | g gaa gaa gca aa<br>t Glu Glu Ala As<br>175 |                            |  |  |  |  |  |
| ctt aca aaa tat<br>Leu Thr Lys Tyn<br>180   | gga tct aaa<br>Gly Ser Lys          | gtg tat ata at<br>Val Tyr Ile Il<br>185     | c cat agg aga ga<br>e His Arg Arg As<br>190 | t gct 2133<br>p Ala        |  |  |  |  |  |
| ttt aga gcg tct<br>Phe Arg Ala Ser<br>195   | aag att atg<br>Lys Ile Met<br>200   | : Gln Gln Arg Al                            | t ttg tct aat cc<br>a Leu Ser Asn Pr<br>205 | t aag 2181<br>o Lys        |  |  |  |  |  |
|   |                                     |   | a gct tat gga ga<br>u Ala Tyr Gly As<br>)   |                            |  |  |  |  |  |
|   |                                     |   | g aat gtg gtt ac<br>s Asn Val Val Th<br>24  | r Gly                      |  |  |  |  |  |
|   | Leu Lys Val                         |   | e ttt gct att gg<br>e Phe Ala Ile Gl<br>255 |                            |  |  |  |  |  |
| gag cca gct acc<br>Glu Pro Ala Thi<br>260   | aag ttt ttg<br>Lys Phe Leu          | ggat ggt ggt gt<br>Asp Gly Gly Va<br>265    | t gag tta gat tc<br>l Glu Leu Asp Se<br>270 | g gat 2373<br>r Asp        |  |  |  |  |  |
| ggt tat gtt gtc<br>Gly Tyr Val Val<br>275   | e acg aag cct<br>Thr Lys Pro<br>280 | Gly Thr Thr Gl                              | g act agc gtt cc<br>n Thr Ser Val Pr<br>285 | c gga 2421<br>o Gly        |  |  |  |  |  |
| gtt ttc gct gcg<br>Val Phe Ala Ala<br>290   | ggt gat gtt<br>Gly Asp Val<br>295   | cag gat aag aag<br>Gln Asp Lys Lys<br>300   | g tat agg caa gc<br>s Tyr Arg Gln Al<br>)   | c atc 2469<br>a Ile<br>305 |  |  |  |  |  |
| act gct gca gga<br>Thr Ala Ala Gly  | act ggg tgc<br>Thr Gly Cys<br>310   | atg gca gct ttg<br>Met Ala Ala Le<br>315    | g gat gca gag ca<br>1 Asp Ala Glu Hi<br>32  | s Tyr                      |  |  |  |  |  |
| tta caa gag att<br>Leu Gln Glu Ile<br>325   | Gly Ser Gln                         | caa ggt aag agt<br>Gln Gly Lys Sei<br>330   | gat tga agetta<br>Asp *                     | ataa 2566                  |  |  |  |  |  |
| gtatgaacta aaatgcatgt aggtgtaaga gctcatggag agcatggaat attgtatccg 2626 accatgtaac agtataataa ctgagctcca tctcacttct tctatgaata aacaaaggat 2686 gttatgatat attaacactc tatctatgca ccttattgtt ctatgataaa tttcctctta 2746 ttattataaa tcatctgaat cgtgacggct tatggaatgc ttcaaatagt acaaaaacaa 2806 atgtgtacta taagactttc taaacaattc taactttagc attgtgaacg agacataagt 2866 gttaagaaga cataacaatt ataatggaag aagtttgtct ccatttatat attatatat 2926 acccacttat gtattatat aggatgttaa aggagacataa caattataaa gagagaaggt 2986 tgtatcatt tatatatta atactacca tttatatatt atactacca tttatatat aggatgttaa aggatcattt gaactctctt actctgtata aggttggat catccttaaa gtgggtctat 3166 ttaattttat tgcttctac agataaaaaa aaaattatga gttggtttga taaaatattg 3226 aaggatttaa aataataata aataataaat aacaatataat aacatataat aatgtatat aaatttatta 3286 ttaatataca tttatcaaca tatttaaca aggagaaag gtgggtccaa accatataca tttattaaca gtgggcaaatg gtgtgtccaa ttttttttt ttatcggcaa ggaaataaaa 3466 ttaaattagg gacaacaaaa aaaacaggcaa gggaaatttt ttaatttggg ttgtcttgtt 3586 tgctgcataa tttatgcagt aaaacaccc tttagcagta gagcaatggt 3646 |                                     |   |   |                            |  |  |  |  |  |

aatgagacac ttcagggatg tttcaaccct tatacaaaac cccaaaaaca agtttcctag 3766 caccctacca actaaggtac c <210> 23 <211> 333 <212> PRT <213> Artificial Sequence <220> <223> Chimeric <400> 23 Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu 20 25 Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly 35 40 Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser 70 Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp 85 90 Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu 100 105 110 Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser 120 125 Phe Val Gly Ser Gly Glu Gly Ser Gly Gly Phe Trp Asn Arg Gly Ile 135 140 Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys 150 155 Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn 170 175 165 Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg Arg Asp 190 180 185 Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro 205 195 200 Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp 215 220 Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr 230 235 Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly 245 250 His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser 265 270 260 Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro 275 280 285 Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala 295 300 Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His 310 315 Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp 325 330 <210> 24 <211> 4546 <212> DNA <213> Artificial Sequence <220> <221> CDS <222> (1555)...(1907)

<221> CDS

<222> (2148)...(3315)

<223> Chimeric

<400> 24 ctgcaggaat tcattgtact cccagtatca ttatagtgaa agttttggct ctctcgccgg 60 tggtttttta cctctattta aaggggtttt ccacctaaaa attctggtat cattctcact 120 ttacttgtta ctttaatttc tcataatctt tggttgaaat tatcacgctt ccgcacacga 180 tatccctaca aatttattat ttgttaaaca ttttcaaacc gcataaaatt ttatgaaqtc 240 ccgtctatct ttaatgtagt ctaacatttt catattgaaa tatataattt acttaatttt 300 agogttggta gaaagcataa tgatttatto ttattottot toatataaat gtttaatata 360 caatataaac aaattottta oottaagaag gatttoccat tttatatttt aaaaatatat 420 ttatcaaata tttttcaacc acgtaaatct cataataata agttgtttca aaagtaataa 480 aatttaactc cataattttt ttattcgact gatcttaaag caacacccag tgacacaact 540 agccattttt ttctttgaat aaaaaaatcc aattatcatt gtatttttt tatacaatga 600 aaatttcacc aaacaatcat ttgtggtatt tctgaagcaa gtcatgttat gcaaaattct 660 ataattccca tttgacacta cggaagtaac tgaagatctg cttttacatg cgagacacat 720 cttctaaagt aattttaata atagttacta tattcaagat ttcatatatc aaatactcaa 780 tattacttct aaaaaattaa ttagatataa ttaaaatatt acttttttaa ttttaagttt 840 aattgttgaa tttgtgacta ttgatttatt attctactat gtttaaattg ttttatagat 900 agtttaaagt aaatataagt aatgtagtag agtgttagag tgttacccta aaccataaac 960 tataagattt atggtggact aattttcata tatttcttat tgcttttacc ttttcttggt 1020 atgtaagtcc gtaactggaa ttactgtggg ttgccatggc actctgtggt cttttggttc 1080 atgcatggat gcttgcgcaa gaaaaagaca aagaacaaag aaaaaagaca aaacagagag 1140 acaaaacgca atcacacaac caactcaaat tagtcactgg ctgatcaaga tcgccgcgtc 1200 catgtatgtc taaatgccat gcaaagcaac acgtgcttaa catgcacttt aaatggctca 1260 cecateteaa eccaeacaea aacacattge ettttette ateateacea caaceacetg 1320 tatatattca ttctcttccg ccacctcaat ttcttcactt caacacacgt caacctgcat 1380 atgcgtgtca tcccatgccc aaatctccat gcatgttcca accaccttct ctcttatata 1440 atacctataa atacctetaa tatcacteac ttettteate atecatecat ceagagtact 1500 actactctac tactataata ccccaaccca actcatattc aatactactc tact atg 1557 Met gcg gat aca gct aga gga acc cat cac gat atc atc ggc aga gac cag 1605 Ala Asp Thr Ala Arg Gly Thr His His Asp Ile Ile Gly Arg Asp Gln 10 tac ccg atg atg ggc cga gac cga gac cag tac cag atg tcc gga cga 1653 Tyr Pro Met Met Gly Arg Asp Arg Asp Gln Tyr Gln Met Ser Gly Arg 20 gga tet gac tac tec aag tet agg cag att get aaa get gea act get 1701 Gly Ser Asp Tyr Ser Lys Ser Arg Gln Ile Ala Lys Ala Ala Thr Ala gtc aca gct ggt ggt tcc ctc ctt gtt ctc tcc agc ctt acc ctt gtt 1749 Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu Val 50 gga act gtc ata gct ttg act gtt gca aca cct ctg ctc gtt atc ttc 1797 Gly Thr Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu Val Ile Phe age cea ate ett gte eeg get ete ate aca gtt gea ete ete ate ace 1845 Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile Thr ggt ttt ctt tcc tct gga ggg ttt ggc att gcc gct ata acc gtt ttc 1893 Gly Phe Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile Thr Val Phe tct tgg att tac aa gtaagcacac atttatcatc ttacttcata attttqtgca 1947 Ser Trp Ile Tyr Lys

atatgtgcat gcatgtgttg agccagtagc tttggatcaa tttttttggt cgaataacaa 2007

| acci       | tagct             | tag (             | cttg       | aatg       | tg t       | ctgt:<br>tac      | gtat:<br>gca      | a tca<br>acg<br>a Th | atct.<br>gga | atat<br>gag | agg<br>cac        | taaa<br>cca       | atg<br>cag<br>o Gl | cttg<br>gga | aatttg<br>gtatga<br>tca<br>y Ser |      |
|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|----------------------|--------------|-------------|-------------------|-------------------|--------------------|-------------|----------------------------------|------|
|            |                   |                   |            |            |            |                   | atg<br>Met        |                      |              |             |                   |                   |                    |             |                                  | 2226 |
|            |                   |                   |            |            |            |                   | tac<br>Tyr        |                      |              |             |                   |                   |                    |             |                                  | 2274 |
|            |                   |                   |            |            |            |                   | ggt<br>Gly        |                      |              |             |                   |                   |                    |             |                                  | 2322 |
|            |                   |                   |            |            |            |                   | ctc<br>Leu        |                      |              |             |                   |                   |                    |             |                                  | 2370 |
| gca<br>Ala | cac<br>His        | acg<br>Thr<br>195 | gcg<br>Ala | gcg<br>Ala | att<br>Ile | tac<br>Tyr        | gca<br>Ala<br>200 | gct<br>Ala           | agg<br>Arg   | gct<br>Ala  | gaa<br>Glu        | ctt<br>Leu<br>205 | aaa<br>Lys         | cct<br>Pro  | ctt<br>Leu                       | 2418 |
| ctc<br>Leu | ttc<br>Phe<br>210 | gaa<br>Glu        | gga<br>Gly | tgg<br>Trp | atg<br>Met | gct<br>Ala<br>215 | aac<br>Asn        | gac<br>Asp           | atc<br>Ile   | gct<br>Ala  | ccc<br>Pro<br>220 | ggt<br>Gly        | ggt<br>Gly         | caa<br>Gln  | cta<br>Leu                       | 2466 |
|            |                   |                   |            |            |            |                   | aat<br>Asn        |                      |              |             |                   |                   |                    |             |                                  | 2514 |
|            |                   |                   |            |            |            |                   | aaa<br>Lys        |                      |              |             |                   |                   |                    |             |                                  | 2562 |
| Gly        | Thr               | Thr               | 11e<br>260 | Phe        | Thr        | Glu               | acg<br>Thr        | Val<br>265           | Thr          | Lys         | Val               | Āsp               | Phe<br>270         | Ser         | Ser                              | 2610 |
| Lys        | Pro               | Phe<br>275        | Lys        | Leu        | Phe        | Thr               | gat<br>Asp<br>280 | Ser                  | Lys          | Ala         | Ile               | Leu<br>285        | Ala                | Āsp         | Ala                              | 2658 |
| Val        | Ile<br>290        | Leu               | Ala        | Thr        | Gly        | Ala<br>295        | gtg<br>Val        | Ala                  | Lys          | Arg         | Leu<br>300        | Ser               | Phe                | Val         | Gly                              | 2706 |
|            |                   |                   |            |            |            |                   | ttc<br>Phe        |                      |              |             |                   |                   |                    |             |                                  | 2754 |
|            |                   |                   |            |            |            |                   | ecg<br>Pro        |                      |              |             |                   |                   |                    |             |                                  | 2802 |
|            |                   |                   |            |            |            |                   | gca<br>Ala        |                      |              |             |                   |                   |                    |             |                                  | 2850 |
|            |                   |                   |            |            |            |                   | ata<br>Ile<br>360 |                      |              |             |                   |                   |                    |             |                                  |      |
| gcg        | tct               | aag               | att        | atg        | cag        | cag               | cga               | gct                  | ttg          | tct         | aat               | cct               | aag                | att         | gat                              | 2946 |

```
Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro Lys Ile Asp
gtg att tgg aac tcg tct gtt gtg gaa gct tat gga gat gga gaa aga
                                                                       2994
Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp Gly Glu Arg
                     390
gat gtg ctt gga gga ttg aaa gtg aag aat gtg gtt acc gga gat gtt
                                                                       3042
Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr Gly Asp Val
                                                                       3090
tot gat tta aaa gtt tot gga ttg tto ttt got att ggt cat gag coa
Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly His Glu Pro
             420
                                                       430
gct acc aag ttt ttg gat ggt ggt gtt gag tta gat tcg gat ggt tat Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser Asp Gly Tyr
                                                                      3138
gtt gtc acg aag cct ggt act aca cag act agc gtt ccc gga gtt ttc
                                                                      3186
Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro Gly Val Phe
gct gcg ggt gat gtt cag gat aag aag tat agg caa gcc atc act gct
                                                                      3234
Ala Ala Gly Asp .Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala
gca gga act ggg tgc atg gca gct ttg gat gca gag cat tac tta caa
                                                                      3282
Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His Tyr Leu Gln
gag att gga tct cag caa ggt aag agt gat tga agcttaataa gtatgaacta 3335
Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp
aaatgcatgt aggtgtaaga gctcatggag agcatggaat attgtatccg accatgtaac 3395 agtataataa ctgagctcca tctcacttct tctatgaata aacaaaggat gttatgatat 3455
attaacacte tatetatgca cettattgtt etatgataaa ttteetetta ttattataaa 3515
tcatctgaat cgtgacggct tatggaatgc ttcaaatagt acaaaaacaa atgtgtacta 3575
taagactttc taaacaattc taactttagc attgtgaacg agacataagt gttaagaaga 3635
cataacaatt ataatggaag aagtttgtct ccatttatat attatatatt acccacttat 3695 gtattatatt aggatgttaa ggagacataa caattataaa gagagaagtt tgtatccatt 3755
tatatattat atactaccca titatatatt atacttatcc acttattiaa tgtctttata 3815
aggtttgatc catgatattt ctaatatttt agttgatatg tatatgaaag ggtactattt 3875
gaactetett actetgtata aaggttggat catcettaaa gtgggtetat ttaattttat 3935
tgettettae agataaaaaa aaaattatga gttggtttga taaaatattg aaggatttaa 3995
aataataata aataataaat aacatataat atatgtatat aaatttatta taatataaca 4055
tttatctata aaaaagtaaa tattgtcata aatctataca atcgtttagc cttgctggac 4115
gacteteaat tatttaaaeg agagtaaaea tatttgaett tttggttatt taacaaatta 4175
ttatttaaca ctatatgaaa ttttttttt ttatcggcaa ggaaataaaa ttaaattagg 4235
agggacaatg gtgtgtccca atccttatac aaccaacttc cacaggaagg tcaggtcggg 4295
gacaacaaaa aaacaggcaa gggaaatttt ttaatttggg ttgtcttgtt tgctgcataa 4355
ttcagggatg tttcaaccct tatacaaaac cccaaaaaca agtttcctag caccctacca 4535
actaaggtac c
<210> 25
<211> 118
<212> PRT
<213> Artificial Sequence
<220>
<223> Chimeric
```

<400> 25 Met Ala Asp Thr Ala Arg Gly Thr His His Asp Ile Ile Gly Arg Asp

<210> 26 <211> 388 <212> PRT <213> Artificial Sequence

<220> <223> Chimeric

<400> 26 Tyr Ala Thr Gly Glu His Pro Gln Gly Ser Asp Lys Leu Asp Ser Ala Arg Met Lys Leu Gly Ser Lys Ala Gln Asp Leu Lys Asp Arg Ala Gln 20 Tyr Tyr Gly Gln Gln His Thr Gly Gly Glu His Asp Arg Asp Arg Thr 40 Arg Gly Gln His Thr Thr Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile 70 75 Tyr Ala Ala Arg Ala Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met 90 95 Ala Asn Asp Ile Ala Pro Gly Gly Gln Leu Thr Thr Thr Thr Asp Val 100 105 Glu Asn Phe Pro Gly Phe Pro Glu Gly Ile Leu Gly Val Glu Leu Thr 115 120 Asp Lys Phe Arg Lys Gln Ser Glu Arg Phe Gly Thr Thr Ile Phe Thr 135 140 Glu Thr Val Thr Lys Val Asp Phe Ser Ser Lys Pro Phe Lys Leu Phe 155 150 Thr Asp Ser Lys Ala Ile Leu Ala Asp Ala Val Ile Leu Ala Thr Gly 170 Ala Val Ala Lys Arg Leu Ser Phe Val Gly Ser Gly Glu Gly Ser Gly 185 Gly Phe Trp Asn Arg Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala 195 200 Ala Pro Ile Phe Arg Asn Lys Pro Leu Ala Val Ile Gly Gly Asp 215 220 Ser Ala Met Glu Glu Ala Asn Phe Leu Thr Lys Tyr Gly Ser Lys Val 230 235 Tyr Ile Ile His Arg Arg Asp Ala Phe Arg Ala Ser Lys Ile Met Gln 245 250 Gln Arg Ala Leu Ser Asn Pro Lys Ile Asp Val Ile Trp Asn Ser Ser 265 270 Val Val Glu Ala Tyr Gly Asp Gly Glu Arg Asp Val Leu Gly Gly Leu 275 280 285 Lys Val Lys Asn Val Val Thr Gly Asp Val Ser Asp Leu Lys Val Ser 295 Gly Leu Phe Phe Ala Ile Gly His Glu Pro Ala Thr Lys Phe Leu Asp 315 Gly Gly Val Glu Leu Asp Ser Asp Gly Tyr Val Val Thr Lys Pro Gly

```
325
                                     330
                                                           335
Thr Thr Gln Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln
                                 345
                                                      350
Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala Ala Gly Thr Gly Cys Met
                             360
                                                  365
Ala Ala Leu Asp Ala Glu His Tyr Leu Gln Glu Ile Gly Ser Gln Gln
                         375
    370
Gly Lys Ser Asp
385
<210> 27
<211> 4545
<212> DNA
<213> Artificial Sequence
<220>
<223> Chimeric
<221> CDS
<222> (1555)...(2906)
<221> CDS
<222> (3147) ... (3315)
ctgcaggaat tcattgtact cccagtatca ttatagtgaa agttttggct ctctcgccgg 60
tggtttttta cctctattta aaggggtttt ccacctaaaa attctggtat cattctcact 120
ttacttgtta ctttaatttc tcataatctt tggttgaaat tatcacgctt ccgcacacga 180
tatccctaca aatttattat ttgttaaaca ttttcaaacc gcataaaatt ttatgaagtc 240
ccgtctatct ttaatgtagt ctaacatttt catattgaaa tatataattt acttaatttt 300
agogttggta gaaagcataa tgatttattc ttattcttct tcatataaat gtttaatata 360
caatataaac aaattottta oottaagaag gatttoccat tttatatttt aaaaatatat 420
ttatcaaata tttttcaacc acgtaaatct cataataata agttgtttca aaagtaataa 480
aatttaactc cataattttt ttattcgact gatcttaaag caacacccag tgacacaact 540
agccattttt ttctttgaat aaaaaaatcc aattatcatt gtatttttt tatacaatga 600 aaatttcacc aaacaatcat ttgtggtatt tctgaagcaa gtcatgttat gcaaaattct 660
ataatteeca tttgacacta eggaagtaac tgaagatetg ettttacatg egagacacat 720
cttctaaagt aatittaata atagttacta tattcaagat ttcatatatc aaatactcaa 780
tattacttct aaaaaattaa ttagatataa ttaaaatatt acttttttaa ttttaagttt 840
aattgttgaa tttgtgacta ttgatttatt attctactat gtttaaattg ttttatagat 900
agtttaaagt aaatataagt aatgtagtag agtgttagag tgttacccta aaccataaac 960 tataagattt atggtggact aattttcata tatttcttat tgcttttacc ttttcttggt 1020
atgtaagtcc gtaactggaa ttactgtggg ttgccatggc actctgtggt cttttggttc 1080
atgcatggat gcttgcgcaa gaaaaagaca aagaacaaag aaaaaagaca aaacagagag 1140
acaaaacgca atcacacac caactcaaat tagtcactgg ctgatcaaga tcgccgcgtc 1200
catgtatgtc taaatgccat gcaaagcaac acgtgcttaa catgcacttt aaatggctca 1260
cccatctcaa cccacacaca aacacattgc ctttttcttc atcatcacca caaccacctg 1320
tatatattca ttctcttccg ccacctcaat ttcttcactt caacacacgt caacctgcat 1380
atgegtgtca teccatgeec aaateteeat geatgtteea accacettet etettatata 1440
actactctac tactataata ccccaaccca actcatattc aatactactc tact atg
                                                              Met
aat ggt ctc gaa act cac aac aca agg ctc tgt atc gta gga agt ggc
                                                                    1605 '
Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser Gly
                                                                    1653
cca gcg gca cac acg gcg gcg att tac gca gct agg gct gaa ctt aaa
Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu Lys
         20
cct ctt ctc ttc gaa gga tgg atg gct aac gac atc gct ccc ggt ggt
                                                                    1701
Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly Gly
```

| caa<br>Gln<br>50  | cta<br>Leu        | aca<br>Thr        | acc<br>Thr        | acc<br>Thr        | acc<br>Thr<br>55  | gac<br>Asp        | gtc<br>Val        | gag<br>Glu        | aat<br>Asn        | ttc<br>Phe<br>60  | ccc<br>Pro        | gga<br>Gly        | ttt<br>Phe        | cca<br>Pro        | gaa<br>Glu<br>65  | 1749   |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------|
| ggt<br>Gly        | att<br>Ile        | ctc<br>Leu        | gga<br>Gly        | gta<br>Val<br>70  | gag<br>Glu        | ctc<br>Leu        | act<br>Thr        | gac<br>Asp        | aaa<br>Lys<br>75  | ttc<br>Phe        | cgt<br>Arg        | aaa<br>Lys        | caa<br>Gln        | tcg<br>Ser<br>80  | gag<br>Glu        | . 1797 |
| cga<br>Arg        | ttc<br>Phe        | ggt<br>Gly        | act<br>Thr<br>85  | acg<br>Thr        | ata<br>Ile        | ttt<br>Phe        | aca<br>Thr        | gag<br>Glu<br>90  | acg<br>Thr        | gtg<br>Val        | acg<br>Thr        | aaa<br>Lys        | gtc<br>Val<br>95  | gat<br>Asp        | ttc<br>Phe        | 1845   |
| tct<br>Ser        | tcg<br>Ser        | aaa<br>Lys<br>100 | ccg<br>Pro        | ttt<br>Phe        | aag<br>Lys        | cta<br>Leu        | ttc<br>Phe<br>105 | aca<br>Thr        | gat<br>Asp        | tca<br>Ser        | aaa<br>Lys        | gcc<br>Ala<br>110 | att<br>Ile        | ctc<br>Leu        | gct<br>Ala        | 1893   |
| gac<br>Asp        | gct<br>Ala<br>115 | gtg<br>Val        | att<br>Ile        | ctc<br>Leu        | gct<br>Ala        | act<br>Thr<br>120 | gga<br>Gly        | gct<br>Ala        | gtg<br>Val        | gct<br>Ala        | aag<br>Lys<br>125 | cgg<br>Arg        | ctt<br>Leu        | agc<br>Ser        | ttc<br>Phe        | 1941   |
| gtt<br>Val<br>130 | gga<br>Gly        | tct<br>Ser        | ggt<br>Gly        | gaa<br>Glu        | ggt<br>Gly<br>135 | tct<br>Ser        | gga<br>Gly        | ggt<br>Gly        | ttc<br>Phe        | tgg<br>Trp<br>140 | aac<br>Asn        | cgt<br>Arg        | gga<br>Gly        | atc<br>Ile        | tcc<br>Ser<br>145 | 1989   |
|                   |                   |                   |                   |                   | gac<br>Asp        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 2037   |
|                   |                   |                   |                   |                   | gga<br>Gly        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 2085   |
|                   |                   |                   |                   |                   | tct<br>Ser        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 2133   |
|                   |                   |                   |                   |                   | att<br>Ile        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 2181   |
|                   |                   |                   |                   |                   | aac<br>Asn<br>215 |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 2229   |
| gaa<br>Glu        | aga<br>Arg        | gat<br>Asp        | gtg<br>Val        | ctt<br>Leu<br>230 | gga<br>Gly        | gga<br>Gly        | ttg<br>Leu        | aaa<br>Lys        | gtg<br>Val<br>235 | aag<br>Lys        | aat<br>Asn        | gtg<br>Val        | gtt<br>Val        | acc<br>Thr<br>240 | gga<br>Gly        | 2277   |
| gat<br>Asp        | gtt<br>Val        | tct<br>Ser        | gat<br>Asp<br>245 | tta<br>Leu        | aaa<br>Lys        | gtt<br>Val        | tct<br>Ser        | gga<br>Gly<br>250 | ttg<br>Leu        | ttc<br>Phe        | ttt<br>Phe        | gct<br>Ala        | att<br>Ile<br>255 | gly               | cat<br>His        | 2325   |
| gag<br>Glu        | cca<br>Pro        | gct<br>Ala<br>260 | acc<br>Thr        | aag<br>Lys        | ttt<br>Phe        | ttg<br>Leu        | gat<br>Asp<br>265 | ggt<br>Gly        | ggt<br>Gly        | gtt<br>Val        | gag<br>Glu        | tta<br>Leu<br>270 | gat<br>Asp        | tcg<br>Ser        | gat<br>Asp        | 2373   |
| ggt<br>Gly        | tat<br>Tyr<br>275 | gtt<br>Val        | gtc<br>Val        | acg<br>Thr        | aag<br>Lys        | cct<br>Pro<br>280 | ggt<br>Gly        | act<br>Thr        | aca<br>Thr        | cag<br>Gln        | act<br>Thr<br>285 | agc<br>Ser        | gtt<br>Val        | ccc<br>Pro        | gga<br>Gly        | 2421   |
| gtt<br>Val<br>290 | ttc<br>Phe        | gct<br>Ala        | gcg<br>Ala        | ggt<br>Gly        | gat<br>Asp<br>295 | gtt<br>Val        | cag<br>Gln        | gat<br>Asp        | aag<br>Lys        | aag<br>Lys<br>300 | tat<br>Tyr        | agg<br>Arg        | caa<br>Gln        | gcc<br>Ala        | atc<br>Ile<br>305 | 2469   |
|                   |                   |                   |                   |                   | gly<br>ggg        |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   | 2517   |

| tta caa<br>Leu Gln                       |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 2565 |
|--|-------------------|---------------------|-------------------|---------------|---------------------|-----------------------------|------------|----------------------|-------------------|---------------------|-----------------------------|---------------------|-----------------------|------------------|------|
| gct aga<br>Ala Arg                       | gga<br>Gly<br>340 | acc<br>Thr          | cat<br>His        | cac<br>His    | gat<br>Asp          | atc<br>Ile<br>345           | atc<br>Ile | ggc<br>Gly           | aga<br>Arg        | gac<br>Asp          | cag<br>Gln<br>350           | tac<br>Tyr          | ccg<br>Pro            | atg<br>Met       | 2613 |
| atg ggc<br>Met Gly<br>355                |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 2661 |
| tac tcc<br>Tyr Ser<br>370                |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 2709 |
| ggt ggt<br>Gly Gly                       |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 2757 |
| ata gct<br>Ile Ala                       |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 2805 |
| ctt gtc<br>Leu Val                       |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 2853 |
| tcc tct<br>Ser Ser<br>435                |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 2901 |
| tac aa q<br>Tyr Lys<br>450               | gtaag             | caca                | ac at             | ttat          | cato                | : tta                       | actto      | cata                 | attt              | tgtg                | jca a                       | ıtatç               | gtgca                 | ıt               | 2956 |
| gcatgtg<br>aagaaat<br>cttgaat<br>ttgtgaa | tgc a<br>gtg t    | aatt<br>ctgt<br>tac | ctac<br>gtat      | gg ga<br>a to | acat<br>atct<br>gga | ttgg<br>atat<br>gag<br>y Gl | tta<br>agg | acta<br>gtaaa<br>cca | aat<br>atg<br>cag | acga<br>cttg<br>gga | aatt<br>gtat<br>tca<br>y Se | tg a<br>ga t<br>gac | accta<br>acct<br>acct | igctag<br>:attga | 3076 |
| gac agt<br>Asp Ser<br>465                |                   |                     |                   |               |                     |                             |            |                      |                   |                     |                             |                     |                       |                  | 3234 |
| aga gct<br>Arg Ala                       | cag<br>Gln        | tac<br>Tyr          | tac<br>Tyr<br>485 | gga<br>Gly    | cag<br>Gln          | caa<br>Gln                  | cat<br>His | act<br>Thr<br>490    | ggt<br>Gly        | gly<br>aaa          | gaa<br>Glu                  | cat<br>His          | gac<br>Asp<br>495     | cgt<br>Arg       | 3282 |
|  | act               | cgt                 | ggt               | ggc           | cag                 | cac                         | act        | act                  | taa               | gctt                | aata                        | ag t                | atga                  | actaa            | 3335 |
| gac cgt<br>Asp Arg                       |                   | Arg<br>500          | Gly               | Gly           | Gln                 | His                         | Thr<br>505 | Thr                  | *                 |                     |                             |                     |                       |                  |      |

```
ataataataa ataataaata acatataata tatgtatata aatttattat aatataacat 4055
ttatctataa aaaagtaaat attgtcataa atctatacaa tcgtttagcc ttgctggacg 4115
actctcaatt atttaaacga gagtaaacat atttgacttt ttggttattt aacaaattat 4175
tatttaacac tatatgaaat ttitttttt tatcggcaag gaaataaaat taaattagga 4235
gggacaatgg tgtgtcccaa tccttataca accaacttcc acaggaaggt caggtcgggg 4295
acaacaaaaa aacaggcaag ggaaattttt taatttgggt tgtcttgttt gctgcataat 4355
ttatgcagta aaacactaca cataaccett ttagcagtag agcaatggtt gaccgtgtgc 4415
tcagggatgt ttcaaccett atacaaaacc ccaaaaacaa gtttcctagc accetaccaa 4535
ctaaggtacc
<210> 28
<211> 451
<212> PRT
<213> Artificial Sequence
<220>
<223> Chimeric
<400> 28
Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser
Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu
           20
                               25
Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly
                           40
Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro
                       55
Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser
Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp
                                   90
               85
Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu
           100
                               105
Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser
                           120
Phe Val Gly Ser Gly Glu Gly Ser Gly Gly Phe Trp Asn Arg Gly Ile
                       135
                                           140
   130
Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys
                   150
                                       155
Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn
               165
                                   170
                                                       175
Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile İle His Arg Arg Asp
           180
                               185
                                                   190
Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro
                           200
Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp
   210
                       215
                                           220
Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr
                   230
                                       235
Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly
                                   250
               245
His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser
                               265
                                                   270
           260
Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro
       275
                           280
                                               285
Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala
   290
                       295
                                           300
Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His
                                       315
                   310
Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp Met Ala Asp
               325
                                   330
                                                       335
Thr Ala Arg Gly Thr His His Asp Ile Ile Gly Arg Asp Gln Tyr Pro
           340
Met Met Gly Arg Asp Arg Asp Gln Tyr Gln Met Ser Gly Arg Gly Ser
                           360
Asp Tyr Ser Lys Ser Arg Gln Ile Ala Lys Ala Ala Thr Ala Val Thr
```

```
375
                                                  380
 Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu Val Gly Thr
                       390
                                              395
 Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu Val Ile Phe Ser Pro
                   405
                                         410
 Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile Thr Gly Phe
              420
                                     425
                                                           430
 Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile Thr Val Phe Ser Trp
          435
                                440
 Ile Tyr Lys
     450
 <210> 29
 <211> 55
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Chimeric
 <400> 29
 Tyr Ala Thr Gly Glu His Pro Gln Gly Ser Asp Lys Leu Asp Ser Ala
  1
                                         10
 Arg Met Lys Leu Gly Ser Lys Ala Gln Asp Leu Lys Asp Arg Ala Gln
              20
                                     25
                                                           30
 Tyr Tyr Gly Gln Gln His Thr Gly Glu His Asp Arg Asp Arg Thr
         35
                                40
 Arg Gly Gly Gln His Thr Thr
     50
 <210> 30
 <211> 4922
 <212> DNA
 <213> Artificial Sequence
 <220>
<221> CDS
 <222> (1555)...(1907)
 <221> CDS
 <222> (2148) ... (3690)
 <223> Chimeric
 <400> 30
ctgcaggaat tcattgtact cccagtatca ttatagtgaa agttttggct ctctcgccgg 60
 tggtttttta cctctattta aaggggtttt ccacctaaaa attctggtat cattctcact 120
ttacttgtta ctttaatttc tcataatctt tggttgaaat tatcacgctt ccgcacacga 180
tatccctaca aatttattat ttgttaaaca ttttcaaacc gcataaaatt ttatgaagtc 240 ccgtctatct ttaatgtagt ctaacatttt catattgaaa tatataattt acttaatttt 300
agegttggta gaaageataa tgatttatte ttattettet teatataaat gtttaatata 360
 caatataaac aaattettta cettaagaag gattteecat tttatatttt aaaaatatat 420
ttatcaaata tttttcaacc acgtaaatct cataataata agttgtttca aaagtaataa 480
aatttaactc cataattttt ttattcgact gatcttaaag caacacccag tgacacaact 540 agccattttt ttctttgaat aaaaaaatcc aattatcatt gtatttttt tatacaatga 600
aaatttcacc aaacaatcat ttgtggtatt tctgaagcaa gtcatgttat gcaaaattct 660
ataattccca tttgacacta cggaagtaac tgaagatctg cttttacatg cgagacacat 720
cttctaaagt aattttaata atagttacta tattcaagat ttcatatatc aaatactcaa 780
tattacttct aaaaaattaa ttagatataa ttaaaatatt acttttttaa ttttaagttt 840
aattgttgaa tttgtgacta ttgatttatt attctactat gtttaaattg ttttatagat 900
agtttaaagt aaatataagt aatgtagtag agtgttagag tgttacccta aaccataaac 960 tataagattt atggtggact aattttcata tatttcttat tgcttttacc ttttcttggt 1020
atgtaagtcc gtaactggaa ttactgtggg ttgccatggc actctgtggt cttttggttc 1080
atgcatggat gcttgcgcaa gaaaaagaca aagaacaaag aaaaaagaca aaacagagag 1140
acaaaacgca atcacacaac caactcaaat tagtcactgg ctgatcaaga tcgccgcgtc 1200
```

| catgtatgtc taaatgccat gcaaagcaac acgtgcttaa catgcacttt aaatggctca 126 cccatctcaa cccacacaa aacacattgc ctttttcttc atcatcacca caaccacctg 132 tatatattca ttctcttccg ccacctcaat ttcttcactt caacacacgt caacctgcat 138 atgcgtgtca tcccatgccc aaatctccat gcatgttcca accaccttct ctcttatata 144 atacctataa atacctctaa tatcactcac ttctttcatc atccatcc | 0 0 0  |
|---|--------|
| gcg gat aca gct aga gga acc cat cac gat atc atc ggc aga gac cag 1609<br>Ala Asp Thr Ala Arg Gly Thr His His Asp Ile Ile Gly Arg Asp Gln<br>5 10 15  | 5      |
| tac ccg atg atg ggc cga gac cga gac cag tac cag atg tcc gga cga 1655<br>Tyr Pro Met Met Gly Arg Asp Arg Asp Gln Tyr Gln Met Ser Gly Arg<br>20 25 30   | 3      |
| gga tct gac tac tcc aag tct agg cag att gct aaa gct gca act gct 1703<br>Gly Ser Asp Tyr Ser Lys Ser Arg Gln Ile Ala Lys Ala Ala Thr Ala<br>35 40 45   | 1      |
| gtc aca gct ggt ggt tcc ctc ctt gtt ctc tcc agc ctt acc ctt gtt Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu Val 50 65   | 9      |
| gga act gtc ata gct ttg act gtt gca aca cct ctg ctc gtt atc ttc Gly Thr Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu Val Ile Phe 70 75 80  | 7      |
| age cca atc ctt gtc ccg gct ctc atc aca gtt gca ctc ctc atc acc Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile Thr 85 90 95  | 5      |
| ggt ttt ctt tcc tct gga ggg ttt ggc att gcc gct ata acc gtt ttc 1893<br>Gly Phe Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile Thr Val Phe<br>100 105 110  | 3      |
| tct tgg att tac aa gtaagcacac atttatcatc ttacttcata attttgtgca 194°.<br>Ser Trp Ile Tyr Lys<br>115  | 7      |
| atatgtgcat gcatgtgttg agccagtagc tttggatcaa tttttttggt cgaataacaa 2007 atgtaacaat aagaaattgc aaattctagg gaacatttgg ttaactaaat acgaaatttg 2067 acctagctag cttgaatgtg tctgtgtata tcatctatat aggtaaaatg cttggtatga 2127 tacctattga ttgtgaatag g tac gca acg gga gag cac cca cag gga tca 2178 Tyr Ala Thr Gly Glu His Pro Gln Gly Ser 120       | 7<br>7 |
| gac aag ttg gac agt gca agg atg aag ttg gga agc aaa gct cag gat 2226<br>Asp Lys Leu Asp Ser Ala Arg Met Lys Leu Gly Ser Lys Ala Gln Asp<br>130 135 140  | 5      |
| ctg aaa gac aga gct cag tac tac gga cag caa cat act ggt ggg gaa 2274 Leu Lys Asp Arg Ala Gln Tyr Tyr Gly Gln Gln His Thr Gly Gly Glu 145 150 160  | 1      |
| cat gac cgt gac cgt act cgt ggt ggc cag cac act acc atg aac acc His Asp Arg Asp Arg Thr Arg Gly Gly Gln His Thr Thr Met Asn Thr 165 170 175   | 2      |
| act cct tct gcg cat gag acg ata cac gaa gtg atc gtt att ggc tcc Thr Pro Ser Ala His Glu Thr Ile His Glu Val Ile Gly Ser 180 185 190   | )      |
| ggt cca gca ggc tac act gct gcc ctg tac gcc gct cgt gca cag cta Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Ala Ala Arg Ala Gln Leu 195 200 205   | 3      |

| aca<br>Thr        | ccg<br>Pro<br>210 | ctg<br>Leu | gta<br>Val        | ttt<br>Phe        | gag<br>Glu        | ggt<br>Gly<br>215 | acc<br>Thr | tca<br>Ser        | ttc<br>Phe        | ggc<br>Gly        | ggc<br>Gly<br>220 | gcg<br>Ala | ctg<br>Leu         | atg<br>Met        | acc<br>Thr        | 2466 |
|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|--------------------|-------------------|-------------------|------|
| acc<br>Thr<br>225 | acc<br>Thr        | gag<br>Glu | gtg<br>Val        | gaa<br>Glu        | aac<br>Asn<br>230 | tac<br>Tyr        | cca<br>Pro | ggt<br>Gly        | ttt<br>Phe        | cgc<br>Arg<br>235 | aac<br>Asn        | ggc        | ata<br>Ile         | acc<br>Thr        | ggc<br>Gly<br>240 | 2514 |
|                   |                   |            |                   | gac<br>Asp<br>245 |                   |                   |            |                   |                   |                   |                   |            |                    |                   |                   | 2562 |
| gaa<br>Glu        | ctg<br>Leu        | cgg<br>Arg | acc<br>Thr<br>260 | gaa<br>Glu        | gac<br>Asp        | gtc<br>Val        | gag<br>Glu | tcg<br>Ser<br>265 | gta<br>Val        | tca<br>Ser        | ttg<br>Leu        | cgt<br>Arg | ggc<br>Gly<br>270  | ccg<br>Pro        | atc.<br>Ile       | 2610 |
|                   |                   |            |                   | acc<br>Thr        |                   |                   |            |                   |                   |                   |                   |            |                    |                   |                   | 2658 |
|                   |                   |            |                   | ggt<br>Gly        |                   |                   |            |                   |                   |                   |                   |            |                    |                   |                   | 2706 |
| caa<br>Gln<br>305 | gaa<br>Glu        | ttg<br>Leu | cta<br>Leu        | gga<br>Gly        | cgt<br>Arg<br>310 | ggc<br>Gly        | gtg<br>Val | agt<br>Ser        | gca<br>Ala        | tgc<br>Cys<br>315 | gcg<br>Ala        | acc<br>Thr | tgc<br>Cys         | gac<br>Asp        | 999<br>Gly<br>320 | 2754 |
|                   |                   |            |                   | ggc<br>Gly<br>325 |                   |                   |            |                   |                   |                   |                   |            |                    |                   |                   | 2802 |
| gcg<br>Ala        | atg<br>Met        | gag<br>Glu | gaa<br>Glu<br>340 | gcc<br>Ala        | ctc<br>Leu        | ttt<br>Phe        | ttg<br>Leu | acc<br>Thr<br>345 | cgg<br>Arg        | ttc<br>Phe        | gcc<br>Ala        | cgc<br>Arg | agc<br>Ser<br>350  | gtc<br>Val        | acg<br>Thr        | 2850 |
|                   |                   |            |                   | cgc<br>Arg        |                   |                   |            |                   |                   |                   |                   |            |                    |                   |                   | 2898 |
| cgc<br>Arg        | gcc<br>Ala<br>370 | cgt<br>Arg | aac<br>Asn        | aat<br>Asn        | gac<br>Asp        | aag<br>Lys<br>375 | atc<br>Ile | aaa<br>Lys        | ttc<br>Phe        | atc<br>Ile        | acc<br>Thr<br>380 | aac<br>Asn | cac<br>His         | acc<br>Thr        | gtg<br>Val        | 2946 |
| gtc<br>Val<br>385 | gcg<br>Ala        | gtg<br>Val | aac<br>Asn        | gly<br>ggg        | tat<br>Tyr<br>390 | aca<br>Thr        | aca<br>Thr | gtg<br>Val        | acc<br>Thr        | gga<br>Gly<br>395 | ttg<br>Leu        | arg<br>Arg | ttg<br>Leu         | cgt<br>Arg        | aac<br>Asn<br>400 | 2994 |
| acc<br>Thr        | aca<br>Thr        | acg<br>Thr | gga<br>Gly        | gag<br>Glu<br>405 | gaa<br>Glu        | acc<br>Thr        | acg<br>Thr | cta<br>Leu        | gta<br>Val<br>410 | gtg<br>Val        | acc<br>Thr        | gly<br>aaa | gtt<br>Val         | ttt<br>Phe<br>415 | gtt<br>Val        | 3042 |
| gca<br>Ala        | att<br>Ile        | ggc<br>Gly | cat<br>His<br>420 | gaa<br>Glu        | cca<br>Pro        | cgt<br>Arg        | tcc<br>Ser | agc<br>Ser<br>425 | ctg<br>Leu        | gtg<br>Val        | agc<br>Ser        | gat<br>Asp | gtc<br>Val<br>430, | Val               | gac<br>Asp        | 3090 |
|                   |                   |            |                   | ggc<br>Gly        |                   |                   |            |                   |                   |                   |                   |            |                    |                   |                   | 3138 |
| tcg<br>Ser        | atg<br>Met<br>450 | gac<br>Asp | ggc<br>Gly        | gtt<br>Val        | ttt<br>Phe        | gcg<br>Ala<br>455 | gcc<br>Ala | ggc<br>Gly        | gac<br>Asp        | ctg<br>Leu        | gta<br>Val<br>460 | gat<br>Asp | cgc<br>Arg         | acc<br>Thr        | tac<br>Tyr        | 3186 |
| cgg<br>Arg        | cag<br>Gln        | gcg<br>Ala | atc<br>Ile        | act<br>Thr        | gcc<br>Ala        | gca<br>Ala        | ggt<br>Gly | agt<br>Ser        | ggc<br>Gly        | tgt<br>Cys        | gcc<br>Ala        | gcc<br>Ala | gcc<br>Ala         | atc<br>Ile        | gac<br>Asp        | 3234 |

| 465   | 470   | 475   | 480  |
|---|---|---|--|
| gcc gaa cgt tgg ttg<br>Ala Glu Arg Trp Let<br>48  | g gcg gag cat gcc ggg<br>u Ala Glu His Ala Gly<br>5 490   | tca aaa gct aac gaa<br>Ser Lys Ala Asn Glu<br>495   | Thr  |
|   | a gac gtt gac agt acc<br>y Asp Val Asp Ser Thr<br>505   |   |  |
| act gcg atg act ga<br>Thr Ala Met Thr As<br>515   | c gcc aag aac gcc ggg<br>p Ala Lys Asn Ala Gly<br>520   | gtc aca ata gaa gtg<br>Val Thr Ile Glu Val<br>525   | acc 3378<br>Thr  |
|   | c gca gac gtc tta tcc<br>e Ala Asp Val Leu Ser<br>535   |   |  |
|   | a aca tgg tgt gga ccc<br>a Thr Trp Cys Gly Pro<br>550   |   |  |
|   | c gcg tcc gaa caa cga<br>e Ala Ser Glu Gln Arg<br>5   |   |  |
|   | c acc aac ccg gaa atg<br>p Thr Asn Pro Glu Met<br>.585  |   |  |
|   | a atg att ctg ttc cag<br>r Met Ile Leu Phe Gln<br>600   |   |  |
|   | t aag ggc aaa gca gcg<br>a Lys Gly Lys Ala Ala<br>615   |   |  |
| gac gtg gta cct aad<br>Asp Val Val Pro Ass<br>625   | c ctc aat taa gctttaaa<br>n Leu Asn *<br>630  | ita agtatgaact aaaat  | gcatg 3720   |
| actgagetee ateteachee etatetatge accettatie tegtgaegge etateggae etateggae etateggae etateggaegaegaegaegaegaegaegaegaegaegaegaega | gga gagcatggaa tattgta ttc ttctatgaat aaacaaa tat tctatgataa atttcct atg cttcaaatag tacaaaa tag cattgtgaac gagacat gtc tccatttata tattata ata acaattataa agagaga tat tatacttatc cacttat ttt tagttgatat gtatate gga tcatccttaa agtgggt taa tatatgtata taaaatt cat aaatctatac aatcgtt aca tatattgacat ttttggt ttt tttatcggca aggaaat atat caaccaactt ccacage ttt tttaattggc ttt tttaagtgagt agagcaa atc agcaaagaat aaataaa aaa ccccaaaaaa aagttto | agga tgttatgata tattatet attatatata atcaract attatatata atcaract attatatatatatatatatatatatatatatatata | aacact 3840 tctgaa 3900 gacttt 3960 aacaat 4020 ttatat 4180 atatta 4140 tttgat 4200 ctctct 4260 ttctta 4320 atctta 4380 atctcaa 4560 gacaat 4620 aacaaa 4680 atgcag 4740 agcttc 4800 agggat 4860 |
| <211> 118<br><212> PRT  |   |   | •  |

<213> Artificial Sequence <220> <223> Chimeric

<400> 31 Met Ala Asp Thr Ala Arg Gly Thr His His Asp Ile Ile Gly Arg Asp 1.0 Gln Tyr Pro Met Met Gly Arg Asp Arg Asp Gln Tyr Gln Met Ser Gly 25 Arg Gly Ser Asp Tyr Ser Lys Ser Arg Gln Ile Ala Lys Ala Ala Thr 40 Ala Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu 55 Val Gly Thr Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu Val Ile 70 75 Phe Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile 85 90 Thr Gly Phe Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile Thr Val 100 105 Phe Ser Trp Ile Tyr Lys

<210> 32 <211> 513 <212> PRT <213> Artificial Sequence <220>

<223> Chimeric

<400> 32 Tyr Ala Thr Gly Glu His Pro Gln Gly Ser Asp Lys Leu Asp Ser Ala Arg Met Lys Leu Gly Ser Lys Ala Gln Asp Leu Lys Asp Arg Ala Gln 25 Tyr Tyr Gly Gln Gln His Thr Gly Glu His Asp Arg Asp Arg Thr 35 40 45 Arg Gly Gly Gln His Thr Thr Met Asn Thr Thr Pro Ser Ala His Glu 55 60 Thr Ile His Glu Val Ile Val Ile Gly Ser Gly Pro Ala Gly Tyr Thr 70 75 Ala Ala Leu Tyr Ala Ala Arg Ala Gln Leu Thr Pro Leu Val Phe Glu 90 Gly Thr Ser Phe Gly Gly Ala Leu Met Thr Thr Thr Glu Val Glu Asn 105 Tyr Pro Gly Phe Arg Asn Gly Ile Thr Gly Pro Glu Leu Met Asp Asp 120 Met Arg Glu Gln Ala Leu Arg Phe Gly Ala Glu Leu Arg Thr Glu Asp 135 140 Val Glu Ser Val Ser Leu Arg Gly Pro Ile Lys Ser Val Val Thr Ala 150 155 Glu Gly Gln Thr Tyr Gln Ala Arg Ala Val Ile Leu Ala Met Gly Thr 165 170 175 Ser Val Arg Tyr Leu Gln Ile Pro Gly Glu Gln Glu Leu Leu Gly Arg 185 Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Ser Phe Phe Arg Gly Gln 200 205 Asp Ile Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Leu 215 220 Phe Leu Thr Arg Phe Ala Arg Ser Val Thr Leu Val His Arg Arg Asp 230 235

Glu Phe Arg Ala Ser Lys Ile Met Leu Gly Arg Ala Arg Asn Asn Asp

Lys Ile Lys Phe Ile Thr Asn His Thr Val Val Ala Val Asn Gly Tyr 260 265 270

250

```
Thr Thr Val Thr Gly Leu Arg Leu Arg Asn Thr Thr Thr Gly Glu Glu
                               280
Thr Thr Leu Val Val Thr Gly Val Phe Val Ala Ile Gly His Glu Pro
                           295
                                                 300
Arg Ser Ser Leu Val Ser Asp Val Val Asp Ile Asp Pro Asp Gly Tyr
305
                      310
                                                                   320
                                             315
Val Leu Val Lys Gly Arg Thr Thr Ser Thr Ser Met Asp Gly Val Phe
                  325
                                        330
Ala Ala Gly Asp Leu Val Asp Arg Thr Tyr Arg Gln Ala Ile Thr Ala
             340
                                    345
Ala Gly Ser Gly Cys Ala Ala Ala Ile Asp Ala Glu Arg Trp Leu Ala
                               360
                                                     365
Glu His Ala Gly Ser Lys Ala Asn Glu Thr Thr Glu Glu Thr Gly Asp
    370
                           375
                                                 380
Val Asp Ser Thr Asp Thr Thr Asp Trp Ser Thr Ala Met Thr Asp Ala
                      390
                                            395
Lys Asn Ala Gly Val Thr Ile Glu Val Thr Asp Ala Ser Phe Phe Ala
                  405
                                        410
                                                              415
Asp Val Leu Ser Ser Asn Lys Pro Val Leu Val Asp Phe Trp Ala Thr
             420
                                    425
                                                          430
Trp Cys Gly Pro Cys Lys Met Val Ala Pro Val Leu Glu Glu Ile Ala
                                                     445
         435
                               440
Ser Glu Gln Arg Asn Gln Leu Thr Val Ala Lys Leu Asp Val Asp Thr
                           455
Asn Pro Glu Met Ala Arg Glu Phe Gln Val Val Ser Ile Pro Thr Met
                      470
                                             475
Ile Leu Phe Gln Gly Gln Pro Val Lys Arg Ile Val Gly Ala Lys
                  485
                                        490
Gly Lys Ala Ala Leu Leu Arg Asp Leu Ser Asp Val Val Pro Asn Leu
             500
                                    505
                                                          510
Asn
<210> 33
<211> 4935
<212> DNA
<213> Artificial Sequence
<220>
<221> CDS
<222> (1554) ... (1906)
<221> CDS
<222> (2147)...(3701)
<223> Chimeric
<400> 33
ctgcaggaat tcattgtact cccagtatca ttatagtgaa agttttggct ctctcgccgg 60
tggtttttta cctctattta aaggggtttt ccacctaaaa attctggtat cattctcact 120 ttacttgtta ctttaatttc tcataatctt tggttgaaat tatcacgctt ccgcacacga 180
tatccctaca aatttattat ttgttaaaca ttttcaaacc gcataaaatt ttatgaagtc 240
ccgtctatct ttaatgtagt ctaacatttt catattgaaa tatataattt acttaatttt 300
agogttggta gaaagcataa agatttattc ttattcttct tcatataaat gtttaatata 360
caatataaac aaattetta eettaagaag gattteeeat tttatatttt aaaaatatat 420 ttateaaata ttttteaacc aegtaaatet eataataata agttgtttea aaagtaataa 480
aatttaactc cataattttt ttattcgact gatcttaaag caacacccag tgacacaact 540
agccattttt ttctttgaat aaaaaaatcc aattatcatt gtatttttt tatacaatga 600
aaatttcacc aaacaatcat ttgtggtatt tctgaagcaa gtcatgttat gcaaaattct 660
ataattccca tttgacacta cggaagtaac tgaagatctg cttttacatg cgagacacat 720
cttctaaagt aattttaata atagttacta tattcaagat ttcatatatc aaatactcaa 780
tattacttct aaaaaattaa ttagatataa ttaaaatatt actttttaa ttttaagttt 840
aattgttgaa tttgtgacta ttgatttatt attctactat gtttaaattg ttttatagat 900
agtttaaagt aaatataagt aatgtagtag agtgttagag tgttacccta aaccataaac 960 tataacattt atggtggact aattttcata tatttcttat tgcttttacc ttttcttggt 1020
atgtaagtee gtaactagaa ttacagtggg ttgecatgge actetgtggt ettttggtte 1080
```

| caa<br>atg<br>cca<br>ata<br>tgc<br>tac | aacg<br>tatg<br>tete<br>tatt<br>gtgt | caa<br>tct<br>aac<br>cat<br>cat<br>aaa | tcac<br>aaat<br>ccac<br>tctc<br>ccca<br>tacc | acaa<br>gcca<br>acac<br>ttcc<br>tgcc<br>tcta | cc a<br>tg c<br>aa a<br>gc c<br>ca a<br>at a | actc<br>aaag<br>caca<br>acct<br>atct<br>tcac | aaat<br>caac<br>ttgc<br>caat<br>ccat<br>tcac | t ag a cg c tt tc g ca t tc    | tcac<br>tgct<br>tttc<br>ttca<br>tgtt<br>tttc | tggc<br>taac<br>ttca<br>cttc<br>ccaa<br>atca | tga<br>atg<br>tca<br>aac<br>cca<br>tcc | tcaa<br>cact<br>tcac<br>acac<br>cctt<br>atcc | gat<br>tta<br>cac<br>gtc<br>ctc<br>atc | cgcc<br>aatg<br>aacc<br>aacc<br>tctt<br>caga<br>act | gagaga<br>gcgtcc<br>gctcac<br>acctgt<br>tgcata<br>atataa<br>gtacta<br>atg<br>Met<br>1 | 1200<br>1260<br>1320<br>1380<br>1440 |
|--|--------------------------------------|--|--|--|--|--|--|--------------------------------|--|--|--|--|--|---|---|--------------------------------------|
|  | gat<br>Asp                           |  |  |  |  |  |  |                                |  |  |  |  |  |   |   | 1604                                 |
|  | ccg<br>Pro                           |  | Met  |  |  |  |  |                                |  |  |  |  |  |   |   | 1652                                 |
|  | tct<br>Ser<br>35                     |  |  |  |  |  |  |                                |  |  |  |  |  |   |   | 1700                                 |
|  | aca<br>Thr                           |  |  |  |  |  |  |                                |  |  |  |  |  |   |   | 1748                                 |
| gga<br>Gly                             | act<br>Thr                           | gtc<br>Val                             | ata<br>Ile                                   | gct<br>Ala<br>70                             | ttg<br>Leu                                   | act<br>Thr                                   | gtt<br>Val                                   | gca<br>Ala                     | aca<br>Thr<br>75                             | cct<br>Pro                                   | ctg<br>Leu                             | ctc<br>Leu                                   | gtt<br>Val                             | atc<br>Ile<br>80                                    | ttc<br>Phe  | 1796                                 |
|  | cca<br>Pro                           |  |  |  |  |  |  |                                |  |  |  |  |  |   |   | 1844                                 |
|  | ttt<br>Phe                           |  |  |  |  |  |  |                                |  |  |  |  |  |   |   | 1892                                 |
|  | tgg<br>Trp<br>115                    |  |  |  | gtaag  | gcaca  | ac at  | ttat                           | cato   | c tta  | actto                                  | cata   | atti                                   | ttgtg   | gca   | 1946                                 |
| atg                                    | taaca                                | aat a                                  | aaga<br>cttg                                 | aattg  | gc as  | tac  | tagg<br>gtata<br>gca                         | g gaa<br>a tca<br>acg<br>a Thi | icati<br>itcta<br>gga                        | tgg<br>atat<br>gag                           | ttaa<br>aggt<br>cac                    | acta<br>aaaa<br>cca                          | at a<br>atg d<br>cag<br>cag            | acgaa<br>ettgg<br>gga                               | aacaa<br>aatttg<br>gtatga<br>tca<br>Ser   | 2066                                 |
|  | aag<br>Lys<br>130                    |  |  |  |  |  |  |                                |  |  |  |  |  |   |   | 2225                                 |
|  | aaa<br>Lys                           |  |  |  |  |  |  |                                |  |  |  |  |  |   |   | 2273                                 |
| cat<br>His                             | gac<br>Asp                           | cgt<br>Arg                             | gac<br>Asp                                   | cgt<br>Arg<br>165                            | act<br>Thr                                   | cgt<br>Arg                                   | ggt<br>Gly                                   | Gly<br>ggc                     | cag<br>Gln<br>170                            | cac<br>His                                   | act<br>Thr                             | acc<br>Thr                                   | atg<br>Met                             | aat<br>Asn<br>175                                   | ggt<br>Gly  | 2321                                 |
| ctc<br>Leu                             | gaa<br>Glu                           | act<br>Thr                             | cac<br>His<br>180                            | aac<br>Asn                                   | aca<br>Thr                                   | agg<br>Arg                                   | ctc<br>Leu                                   | tgt<br>Cys<br>185              | atc<br>Ile                                   | gta<br>Val                                   | gga<br>Gly                             | agt<br>Ser                                   | ggc<br>Gly<br>190                      | cca<br>Pro  | gcg<br>Ala  | 2369                                 |
| gca                                    | cac                                  | acg                                    | gcg  | gcg  | att  | tac  | gca  | gct                            | agg  | gct  | gaa                                    | ctt  | aaa                                    | cct   | ctt   | 2417                                 |

| Ala        | His               | Thr<br>195 | Ala               | Ala        | Ile               | Tyr               | Ala<br>200 | Ala               | Arg        | Ala        | Glu               | Leu<br>205 | Lys               | Pro        | Leu        |      |
|------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|------------|-------------------|------------|-------------------|------------|------------|------|
|            |                   |            |                   |            | atg<br>Met        |                   |            |                   |            |            |                   |            |                   |            | cta<br>Leu | 2465 |
|            |                   |            |                   |            | gtc<br>Val<br>230 |                   |            |                   |            |            |                   |            |                   |            |            | 2513 |
|            | ~~                | -          |                   |            | act<br>Thr        | _                 |            |                   | _          |            |                   | _          |                   | _          |            | 2561 |
| ggt<br>Gly | act<br>Thr        | acg<br>Thr | ata<br>Ile<br>260 | ttt<br>Phe | aca<br>Thr        | gag<br>Glu        | acg<br>Thr | gtg<br>Val<br>265 | acg<br>Thr | aaa<br>Lys | gtc<br>Val        | gat<br>Asp | ttc<br>Phe<br>270 | tct<br>Ser | tcg<br>Ser | 2609 |
|            |                   |            |                   |            | ttc<br>Phe        |                   |            |                   |            |            |                   |            |                   |            |            | 2657 |
| gtg<br>Val | att<br>Ile<br>290 | ctc<br>Leu | gct<br>Ala        | act<br>Thr | gga<br>Gly        | gct<br>Ala<br>295 | gtg<br>Val | gct<br>Ala        | aag<br>Lys | cgg<br>Arg | ctt<br>Leu<br>300 | agc<br>Ser | ttc<br>Phe        | gtt<br>Val | gga<br>Gly | 2705 |
|            |                   |            |                   |            | gga<br>Gly<br>310 |                   |            |                   |            |            |                   |            |                   |            |            | 2753 |
|            |                   |            |                   |            | gct<br>Ala        |                   |            |                   |            |            |                   |            |                   |            |            | 2801 |
| gtg<br>Val | atc<br>Ile        | ggt<br>Gly | gga<br>Gly<br>340 | ggc<br>Gly | gat<br>Asp        | tca<br>Ser        | gca<br>Ala | atg<br>Met<br>345 | gaa<br>Glu | gaa<br>Glu | gca<br>Ala        | aac<br>Asn | ttt<br>Phe<br>350 | ctt<br>Leu | aca<br>Thr | 2849 |
|            |                   |            |                   |            | gtg<br>Val        |                   |            |                   |            |            |                   |            |                   |            |            | 2897 |
| gcg<br>Ala | tct<br>Ser<br>370 | aag<br>Lys | att<br>Ile        | atg<br>Met | cag<br>Gln        | cag<br>Gln<br>375 | cga<br>Arg | gct<br>Ala        | ttg<br>Leu | tct<br>Ser | aat<br>Asn<br>380 | cct<br>Pro | aag<br>Lys        | att<br>Ile | gat<br>Asp | 2945 |
|            |                   |            |                   |            | tct<br>Ser<br>390 |                   |            |                   |            |            |                   |            |                   |            |            | 2993 |
|            |                   |            |                   |            | ttg<br>Leu        |                   |            |                   |            |            |                   |            |                   |            |            | 3041 |
|            |                   |            |                   |            | tct<br>Ser        |                   |            |                   |            |            |                   |            |                   |            |            | 3089 |
|            |                   |            |                   |            | gat<br>Asp        |                   |            |                   |            |            |                   |            |                   |            |            | 3137 |
|            |                   |            |                   |            | ggt<br>Gly        |                   |            |                   |            |            |                   |            |                   |            |            | 3185 |

| gct<br>Ala<br>465  | gcg<br>Ala   | ggt<br>Gly   | gat<br>Asp                             | gtt<br>Val   | cag<br>Gln<br>470   | gat<br>Asp   | aag<br>Lys   | aag<br>Lys                              | tat<br>Tyr  | agg<br>Arg<br>475  | caa<br>Gln   | gcc<br>Ala   | atc<br>Ile                               | act<br>Thr   | gct<br>Ala<br>480  | 3233   |
|--|--|--|--|--|---|--|--|---|---|--|--|--|--|--|--|--|
|  | gga<br>Gly   |  |  |  |   |  |  |   |   |  |  |  |  |  |  | 3281   |
|  | att<br>Ile   |  |  |  |   |  |  |   |   |  |  |  |  |  |  | 3329   |
| gtt<br>Val   | gac<br>Asp   | tcg<br>Ser<br>515  | acg<br>Thr                             | gat<br>Asp   | act<br>Thr  | acg<br>Thr   | gat<br>Asp<br>520  | tgg<br>Trp                              | tcg<br>Ser  | acg<br>Thr   | gct<br>Ala   | atg<br>Met<br>525  | gaa<br>Glu                               | gaa<br>Glu   | gga<br>Gly   | 3377   |
| caa<br>Gln   | gtg<br>Val<br>530  | atc<br>Ile   | gcc<br>Ala                             | tgc<br>Cys   | cac<br>His  | acc<br>Thr<br>535  | gtt<br>Val   | gag<br>Glu                              | aca<br>Thr  | tgg<br>Trp   | aac<br>Asn<br>540  | gag<br>Glu   | cag<br>Gln                               | ctt<br>Leu   | cag<br>Gln   | 3425   |
| aag<br>Lys<br>545  | gct<br>Ala   | aat<br>Asn   | gaa<br>Glu                             | tcc<br>Ser   | aaa<br>Lys<br>550   | act<br>Thr   | ctt<br>Leu   | gtg<br>Val                              | gtg<br>Val  | gtt<br>Val<br>555  | gat<br>Asp   | ttc<br>Phe   | acg<br>Thr                               | gct<br>Ala   | tct<br>Ser<br>560  | 3473   |
| tgg<br>Trp   | tgt<br>Cys   | gga<br>Gly   | cca<br>Pro                             | tgt<br>Cys<br>565  | cgt<br>Arg  | ttc<br>Phe   | atc<br>Ile   | gct<br>Ala                              | cca<br>Pro<br>570   | ttc<br>Phe   | ttt<br>Phe   | gct<br>Ala   | gat<br>Asp                               | ttg<br>Leu<br>575  | gct<br>Ala   | 3521   |
|  | aaa<br>Lys   |  |  |  |   |  |  |   |   |  |  |  |  |  |  | 3569   |
| aag<br>Lys   | tcg<br>Ser   | gtg<br>Val<br>595  | gca<br>Ala                             | agt<br>Ser   | gat<br>Asp  | tgg<br>Trp   | gcg<br>Ala<br>600  | ata<br>Ile                              | cag<br>Gln  | gcg<br>Ala   | atg<br>Met   | cca<br>Pro<br>605  | acc<br>Thr                               | ttc<br>Phe   | atg<br>Met   | 3617   |
|  | ttg<br>Leu<br>610  |  |  |  |   |  |  |   |   |  |  |  |  |  |  | 3665   |
| gat<br>Asp<br>625  | gag<br>Glu   | ctt<br>Leu   | cag<br>Gln                             | tct<br>Ser   | acc<br>Thr<br>630   | att<br>Ile   | gcc<br>Ala   | aaa<br>Lys                              | cac<br>His  | ttg<br>Leu<br>635  | gct<br>Ala   | taag   | getta                                    | aaa  |  | 3711   |
| gate cast cast age tage at the age to a | accat<br>gttat<br>gttat<br>gttat<br>acca<br>gttat<br>ggtac<br>ggtac<br>tgtat<br>aagga<br>cttaa<br>ctaa<br>gc<br>ctaa<br>gc<br>ctaa<br>gc<br>ctaa<br>gc<br>cc<br>cc<br>cc<br>cc<br>cc<br>cc<br>cc<br>cc<br>cc<br>cc<br>cc<br>cc | gt at a state of a sta | aacacacacacacacacacacacacacacacacacaca | gtata<br>ctaaccataac<br>ataac<br>ataaccataactca<br>gette<br>aactcataccata<br>catataccataccataccata | ta character at a control at a | tacted to the control of the control | gaget<br>gacea<br>actac<br>gatgt<br>gatgt<br>cctac<br>gatac<br>cctac<br>actac<br>actac<br>gatac<br>cctac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>acta<br>actac<br>actac<br>actac<br>actac<br>actac<br>acta<br>acta<br>acta<br>actac<br>acta<br>acta<br>acta<br>acta<br>actac<br>acta<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>acta<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>actac<br>acta<br>acta<br>acta<br>acta<br>acta<br>acta<br>actac<br>a<br>acta<br>acta<br>a<br>acta<br>a<br>acta<br>a<br>a<br>a | get | tette<br>tate<br>taagt<br>gaagt<br>tetta<br>aaaaa<br>aaca<br>tagt<br>tatet<br>tagt<br>tatet<br>tatet<br>tagt<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tatet<br>tat<br>ta | act<br>agetta<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>gette<br>g<br>g<br>gette<br>g<br>g<br>g<br>g | tott<br>gttot<br>agea<br>tea<br>atta<br>gata<br>atta<br>atta<br>atta<br>atta | cetatestates at the cetatestatestatestatestatestatestatestat | iga ta a t | ataaa<br>aaatt<br>agtac<br>acgac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>acca<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>accac<br>acca<br>acca<br>accac<br>acca<br>acca<br>acca<br>acca<br>acca<br>acca<br>acca<br>acca<br>accac<br>ac | ttgtat<br>tcaaag<br>tacata<br>tatata<br>tgagata<br>ttatta<br>tgagata<br>ttatta<br>taggtc<br>taaatta<br>cgttt<br>tgaata<br>cgtctt<br>gaaata<br>ttatta<br>tgggtc<br>taatta<br>tcatta<br>tgggtc<br>taatta<br>tcatta<br>tcatta<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcatata<br>tcata<br>tcatata<br>tcatata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tcata<br>tca<br>tc | 3831<br>3891<br>3951<br>4011<br>4071<br>4131<br>4251<br>4311<br>4431<br>4451<br>4671<br>4671<br>4731<br>4791<br>4851 |

```
<211> 118
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (1)...(118)
<223> oleosin
<223> Chimeric
<400> 34
Met Ala Asp Thr Ala Arg Gly Thr His His Asp Ile Ile Gly Arg Asp
                                     10
Gln Tyr Pro Met Met Gly Arg Asp Arg Asp Gln Tyr Gln Met Ser Gly
            20
                                 25
Arg Gly Ser Asp Tyr Ser Lys Ser Arg Gln Ile Ala Lys Ala Ala Thr
        35
                                                  45
                             40
Ala Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu
                         55
                                             60
Val Gly Thr Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu Val Ile
                     70
                                         75
Phe Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile
                                     90
                85
Thr Gly Phe Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile Thr Val
            100
                                 105
Phe Ser Trp Ile Tyr Lys
        115
<210> 35
<211> 518
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (1)...(55)
<223> oleosin
<221> SITE
<222> (56)...(383)
<223> thioredoxin reductase
<221> SITE
<222> (384)...(406)
<223> linker
<221> SITE
<222> (407)...(518)
<223> thioredoxin
<223> Chimeric
<400> 35
Tyr Ala Thr Gly Glu His Pro Gln Gly Ser Asp Lys Leu Asp Ser Ala
                                     10
Arg Met Lys Leu Gly Ser Lys Ala Gln Asp Leu Lys Asp Arg Ala Gln
                                 25
                                                     30
Tyr Tyr Gly Gln Gln His Thr Gly Gly Glu His Asp Arg Asp Arg Thr
        35
                                                 45
                             40
Arg Gly Gly Gln His Thr Thr Met Asn Gly Leu Glu Thr His Asn Thr
                         55
Arg Leu Cys Ile Val Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile
                    70
                                         75
Tyr Ala Ala Arg Ala Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met
```

```
Ala Asn Asp Ile Ala Pro Gly Gly Gln Leu Thr Thr Thr Thr Asp Val
                                105
Glu Asn Phe Pro Gly Phe Pro Glu Gly Ile Leu Gly Val Glu Leu Thr
                            120
Asp Lys Phe Arg Lys Gln Ser Glu Arg Phe Gly Thr Thr Ile Phe Thr
                        135
   130
                                            140
Glu Thr Val Thr Lys Val Asp Phe Ser Ser Lys Pro Phe Lys Leu Phe
                  150
                                        155
Thr Asp Ser Lys Ala Ile Leu Ala Asp Ala Val Ile Leu Ala Thr Gly
                165
                                    170
Ala Val Ala Lys Arg Leu Ser Phe Val Gly Ser Gly Glu Gly Ser Gly
            180
                                185
Gly Phe Trp Asn Arg Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala
        195
                            200
                                                205
Ala Pro Ile Phe Arg Asn Lys Pro Leu Ala Val Ile Gly Gly Gly Asp
                       215
Ser Ala Met Glu Glu Ala Asn Phe Leu Thr Lys Tyr Gly Ser Lys Val
                    230
                                        235
Tyr Ile Ile His Arg Arg Asp Ala Phe Arg Ala Ser Lys Ile Met Gln
               245
                                    250
Gln Arg Ala Leu Ser Asn Pro Lys Ile Asp Val Ile Trp Asn Ser Ser
           260
                                265
Val Val Glu Ala Tyr Gly Asp Gly Glu Arg Asp Val Leu Gly Gly Leu
                            280
Lys Val Lys Asn Val Val Thr Gly Asp Val Ser Asp Leu Lys Val Ser
                        295
                                           300
Gly Leu Phe Phe Ala Ile Gly His Glu Pro Ala Thr Lys Phe Leu Asp
                   310
                                       315
Gly Gly Val Glu Leu Asp Ser Asp Gly Tyr Val Val Thr Lys Pro Gly
                325
                                    330
Thr Thr Gln Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln
           340
                                345
Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala Ala Gly Thr Gly Cys Met
                                               365
       355
                           360
Ala Ala Leu Asp Ala Glu His Tyr Leu Gln Glu Ile Ala Gly Ser Lys
                        375
Ala Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr
                    390 .
                                       395
Thr Asp Trp Ser Thr Ala Met Glu Glu Gly Gln Val Ile Ala Cys His
                405
                                   410
Thr Val Glu Thr Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys
           420
                               425
                                                   430
Thr Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg
       435
                           440
                                               445
Phe Ile Ala Pro Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val
                        455
                                           460
Leu Phe Leu Lys Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp
                   470
                                       475
Trp Ala Ile Gln Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys
               485
                                   490
                                                       495
Ile Leu Asp Lys Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr
           500
                               505
Ile Ala Lys His Leu Ala
       515
```

<210> 36 <211> 458 <212> PRT

<213> Mycobacterium leprae

```
40
Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly
                                            60
Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg
Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg
                                    90
                85
Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala
                                105
                                                    110
Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile
                           120
Pro Gly Glu Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr
                        135
Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly
                    150
                                        155
Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg
                                    170
Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile
                                185
           180
Met Leu Gly Arg Ala Arg Asn Asn Asp Lys Ile Lys Phe Ile Thr Asn
        195
                            200
                                                205
His Thr Val Val Ala Val Asn Gly Tyr Thr Thr Val Thr Gly Leu Arg
Leu Arg Asn Thr Thr Thr Gly Glu Glu Thr Thr Leu Val Val Thr Gly
                    230
                                        235
Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Ser Leu Val Ser Asp
                245
                                    250
Val Val Asp Ile Asp Pro Asp Gly Tyr Val Leu Val Lys Gly Arg Thr
                                265
                                                    270
Thr Ser Thr Ser Met Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp
                            280
Arg Thr Tyr Arg Gln Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala
                       295
                                            300
Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Gly Ser Lys Ala
                    310
                                        315
Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr Thr
                                    330
Asp Trp Ser Thr Ala Met Thr Asp Ala Lys Asn Ala Gly Val Thr Ile
                                345
           340
Glu Val Thr Asp Ala Ser Phe Phe Ala Asp Val Leu Ser Ser Asn Lys
                            360
                                                365
Pro Val Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Lys Met
                        375
                                            380
Val Ala Pro Val Leu Glu Glu Ile Ala Ser Glu Gln Arg Asn Gln Leu
                    390
                                       395
Thr Val Ala Lys Leu Asp Val Asp Thr Asn Pro Glu Met Ala Arg Glu
                405
                                    410
Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gly Gln
                                425
Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg
                            440
Asp Leu Ser Asp Val Val Pro Asn Leu Asn
                   . 455
```

<sup>&</sup>lt;210> 37

<sup>&</sup>lt;211> 471

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Arabidopsis thaliana

<sup>&</sup>lt;220>

<sup>&</sup>lt;223> Chimeric

<sup>&</sup>lt;400> 37

Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser

1 5 10 15
Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu

```
20
                                25
Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly
                            40
Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro
                        55
Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser
                    70
Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp
                85
Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu
           100
                               105
Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser
        115
                            120
                                                125
Phe Val Gly Ser Gly Glu Gly Ser Gly Gly Phe Trp Asn Arg Gly Ile
    130
                        135
                                            140
Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys
                    150
Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn
                165
                                    170
                                                        175
Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg Arg Asp
            180
                                185
Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro
                           200
Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp
                        215
                                            220
Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr
                    230
                                        235
Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly
                245
                                   250
His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser
                                265
Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro
        275
                           280
                                                285
Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala
                        295
                                            300
Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His
                    310
                                        315
Tyr Leu Gln Glu Ile Ala Gly Ser Lys Ala Asn Glu Thr Thr Glu Glu
                325
                                    330
                                                        335
Thr Gly Asp Val Asp Ser Thr Asp Thr Thr Asp Trp Ser Thr Ala Met
           340
                                345
                                                    350
Glu Glu Gly Gln Val Ile Ala Cys Glu Glu Gly Gln Val Ile Ala Cys
       355
                           360
His Thr Val Glu Thr Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser
                       375
                                            380
Lys Thr Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys
                    390
                                       395
Arg Phe Ile Ala Pro Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn
                405
                                    410
Val Leu Phe Leu Lys Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser
           420
                                425
Asp Trp Ala Ile Gln Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly
                            440
       435
                                               445
Lys Ile Leu Asp Lys Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser
                       455
                                            460
Thr Ile Ala Lys His Leu Ala
```

<sup>&</sup>lt;210> 38

<sup>&</sup>lt;211> 345

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Arabidopsis thaliana

<sup>&</sup>lt;220>

<sup>&</sup>lt;221> CDS

<sup>&</sup>lt;222> (1)...(345)

```
atg get teg gaa gaa gga caa gtg ate gee tge cae ace gtt gag aca
                                                                             48
Met Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr
tgg aac gag cag ctt cag aag gct aat gaa tcc aaa act ctt gtg gtg
Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val
                                                                             96
               20
gtt gat tte acg get tet tgg tgt gga eea tgt egt tte ate get eea
                                                                             144
Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro
tto ttt got gat ttg got aag aaa ott oot aac gtg ott tto otc aag
                                                                             192
Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val Leu Phe Leu Lys
      50
gtt gat act gat gaa ttg aag tcg gtg gca agt gat tgg gcg ata cag
Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln
                                                                             240
gcg atg cca acc ttc atg ttt ttg aag gaa ggg aag att ttg gac aaa
                                                                             288
Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys
gtt gtt gga gcc aag aaa gat gag ctt cag tct acc att gcc aaa cac
                                                                             336
Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr Ile Ala Lys His
              100
                                     105
ttg gct taa
                                                                             345
Leu Ala *
```

<210> 39

<211> 114

<212> PRT

<213> Arabidopsis thaliana

<400> 39

Met Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr 10 Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val 25 Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro 45 Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val Leu Phe Leu Lys 55 60 Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln 70 75 Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr Ile Ala Lys His 105 Leu Ala

<210> 40

<211> 999

<212> DNA

<213> Arabidopsis thaliana

<220>

<221> CDS

<222> (1)...(999)

|                   | 0> 4              | -          | ctc               | gaa               | act               | cac               | 220        | 202               | add               | ctc               | tat               | atc        | ata               | gga               | agt.              | 48  |
|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-----|
|                   |                   |            |                   |                   | Thr               |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 10  |
| ggc               | cca<br>Pro        | gcg<br>Ala | gca<br>Ala<br>20  | cac<br>His        | acg<br>Thr        | gcg<br>Ala        | gcg<br>Ala | att<br>Ile<br>25  | tac<br>Tyr        | gca<br>Ala        | gct<br>Ala        | agg<br>Arg | gct<br>Ala<br>30  | gaa<br>Glu        | ctt<br>Leu        | 96  |
|                   |                   |            |                   |                   | gaa<br>Glu        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 144 |
|                   |                   |            |                   |                   | cca<br>Pro        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 192 |
|                   |                   |            |                   |                   | gag<br>Glu<br>70  |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 240 |
|                   |                   |            |                   |                   | ata<br>Ile        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 288 |
|                   |                   |            |                   |                   | aag<br>Lys        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 336 |
|                   |                   |            |                   |                   | gct<br>Ala        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 384 |
|                   |                   |            |                   |                   | gtt<br>Val        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 432 |
| gct<br>Ala<br>145 | tgt<br>Cys        | gct<br>Ala | gtt<br>Val        | tgc<br>Cys        | gac<br>Asp<br>150 | gga<br>Gly        | gct<br>Ala | gct<br>Ala        | ccg<br>Pro        | ata<br>Ile<br>155 | ttc<br>Phe        | cgc<br>Arg | aac<br>Asn        | aaa<br>Lys        | cct<br>Pro<br>160 | 480 |
|                   |                   |            |                   |                   | gga<br>Gly        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 528 |
| ctt<br>Leu        | aca<br>Thr        | aaa<br>Lys | tat<br>Tyr<br>180 | gga<br>Gly        | tct<br>Ser        | aaa<br>Lys        | gtg<br>Val | tat<br>Tyr<br>185 | ata<br>Ile        | atc<br>Ile        | gat<br>Asp        | agg<br>Arg | aga<br>Arg<br>190 | gat<br>Asp        | gct<br>Ala        | 576 |
|                   |                   |            |                   |                   | att<br>Ile        |                   |            |                   |                   |                   |                   |            |                   |                   |                   | 624 |
| att<br>Ile        | gat<br>Asp<br>210 | gtg<br>Val | att<br>Ile        | tgg<br>Trp        | aac<br>Asn        | tcg<br>Ser<br>215 | tct<br>Ser | gtt<br>Val        | gtg<br>Val        | gaa<br>Glu        | gct<br>Ala<br>220 | tat<br>Tyr | gga<br>Gly        | gat<br>Asp        | gga<br>Gly        | 672 |
| gaa<br>Glu<br>225 | aga<br>Arg        | gat<br>Asp | gtg<br>Val        | ctt<br>Leu        | gga<br>Gly<br>230 | gga<br>Gly        | ttg<br>Leu | aaa<br>Lys        | gtg<br>Val        | aag<br>Lys<br>235 | aat<br>Asn        | gtg<br>Val | gtt<br>Val        | acc<br>Thr        | gga<br>Gly<br>240 | 720 |
| gat<br>Asp        | gtt<br>Val        | tct<br>Ser | gat<br>Asp        | tta<br>Leu<br>245 | aaa<br>Lys        | gtt<br>Val        | tct<br>Ser | gga<br>Gly        | ttg<br>Leu<br>250 | ttc<br>Phe        | ttt<br>Phe        | gct<br>Ala | att<br>Ile        | ggt<br>Gly<br>255 | cat<br>His        | 768 |
| gag<br>Glu        | cca<br>Pro        | gct<br>Ala | acc<br>Thr        | aag<br>Lys        | ttt<br>Phe        | ttg<br>Leu        | gat<br>Asp | ggt<br>Gly        | ggt<br>Gly        | gtt<br>Val        | gag<br>Glu        | tta<br>Leu | gat<br>Asp        | tcg<br>Ser        | gat<br>Asp        | 816 |

260 265 270 864 ggt tat gtt gtc acg aag cct ggt act aca cag act agc gtt ccc gga Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro Gly 280 gtt ttc gct gcg ggt gat gtt cag gat aag aag tat agg caa gcc atc 912 Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile 290 295 300 act get gea gga act ggg tgc atg gea get ttg gat gea gag eat tac 960 Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His Tyr 999 tta caa gag att gga tct cag caa ggt aag agt gat tga Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp 325 <210> 41 <211> 332 <212> PRT <213> Arabidopsis thaliana <400> 41 Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu 25 Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly 40 Gly Gln Leu Asn Gln Pro Pro Arg Glu Asn Phe Pro Gly Phe Pro Glu 55 Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser Glu 70 75 Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp Phe 90 Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu Ala 105 Asp Ala Val Ile Leu Ala Ile Gly Ala Val Ala Lys Trp Leu Ser Phe 115 120 125 Val Gly Ser Gly Glu Val Leu Gly Gly Leu Trp Asn Arg Gly Ile Ser 130 135 140 Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys Pro 150 155 Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn Phe 170 165 Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile Asp Arg Arg Asp Ala 180 185 190 Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro Lys 200 Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp Gly 215 220

260 265 270

Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro Gly
275 280 285

Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile
290 295 300

Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr Gly

Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile, Gly His

Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser Asp

230

245

Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His Tyr 305 310 315 320 Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp

250

235

240

255

```
<210> 42
<211> 332
<212> DNA
<213> E. coli
<220>
<221> CDS
<222> (1) ... (332)
<400> 42
atg agc gat aaa att att cac ctg act gac gac agt ttt gac acg gat
                                                                   48
Met Ser Asp Lys Ile Ile His Leu Thr Asp Asp Ser Phe Asp Thr Asp
gta ctc aaa gcg gac ggg gct atc ctc gtt gat ttc tgg gca gag tgg
Val Leu Lys Ala Asp Gly Ala Ile Leu Val Asp Phe Trp Ala Glu Trp
tgc ggg ccg tgt aaa atg atc gct ccg att ctg gat gaa atc gct gac
                                                                   144
Cys Gly Pro Cys Lys Met Ile Ala Pro Ile Leu Asp Glu Ile Ala Asp
gaa tat cag ggc aaa ttg acc gtt gcc aaa ctg aac att gac cag aac
                                                                   192
Glu Tyr Gln Gly Lys Leu Thr Val Ala Lys Leu Asn Ile Asp Gln Asn
                         55
cca ggt act gcg cct aaa tat ggc atc cgc ggt att ccg act ctg ctg
                                                                   240
Pro Gly Thr Ala Pro Lys Tyr Gly Ile Arg Gly Ile Pro Thr Leu Leu
                                                                   288
ctg ttt aaa aac ggc gaa gtg gcg gca acc aaa gta ggc gca ctg tct
Leu Phe Lys Asn Gly Glu Val Ala Ala Thr Lys Val Gly Ala Leu Ser
aaa ggt cag ttg aaa gag ttt ctc gac gcc aat ctg gcg taa ta 🕔
                                                                   332
Lys Gly Gln Leu Lys Glu Phe Leu Asp Ala Asn Leu Ala *
<210> 43
<211> 109
<212> PRT
<213> E. coli
<400> 43
Met Ser Asp Lys Ile Ile His Leu Thr Asp Asp Ser Phe Asp Thr Asp
                                    10
                                                        15
Val Leu Lys Ala Asp Gly Ala Ile Leu Val Asp Phe Trp Ala Glu Trp
            20
                                25
Cys Gly Pro Cys Lys Met Ile Ala Pro Ile Leu Asp Glu Ile Ala Asp
        35
Glu Tyr Gln Gly Lys Leu Thr Val Ala Lys Leu Asn Ile Asp Gln Asn
                        55
                                            60
Pro Gly Thr Ala Pro Lys Tyr Gly Ile Arg Gly Ile Pro Thr, Leu Leu
                    70
                                        75
Leu Phe Lys Asn Gly Glu Val Ala Ala Thr Lys Val Gly Ala Leu Ser
                85
                                    90
Lys Gly Gln Leu Lys Glu Phe Leu Asp Ala Asn Leu Ala
```

<210> 44 <211> 966 <212> DNA <213> E. coli

<220> <221> CDS <222> (1) ... (966) <400> 44 atg ggc acg acc aaa cac agt aaa ctg ctt atc ctg ggt tca ggc ccg Met Gly Thr Thr Lys His Ser Lys Leu Leu Gly Ser Gly Pro geg gga tae ace get get gte tae geg geg ege gee aac etg caa eet Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro gtg ctg att acc ggc atg gaa aaa ggc ggc caa ctg acc acc acc acg 144 Val Leu Ile Thr Gly Met Glu Lys Gly Gly Gln Leu Thr Thr Thr Thr gaa gtg gaa aac tgg cct ggc gat cca aac gat ctg acc ggt ccg tta 192 Glu Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu 240 tta atg gag cgc atg cac gaa cat gcc acc aag ttt gaa act gag atc Leu Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile att ttt gat cat atc aac aag gtg gat ctg caa aac cgt ccg ttc cgt 288 Ile Phe Asp His Ile Asn Lys Val Asp Leu Gln Asn Arg Pro Phe Arg ctg aat ggc gat aac ggc gaa tac act tgc gac gcg ctg att att gcc 336 Leu Asn Gly Asp Asn Gly Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ala 384 acc gga gct tct gca cgc tat ctc ggc ctg ccc tct gaa gaa gcc ttt Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe 115 aaa ggc cgt ggg gtt tct gct tgt gca acc tgc gac ggt ttc ttc tat 432 Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 130 480 cgc aac cag aaa gtt gcg gtc atc ggc ggc ggc aat acc gcg gtt gaa Arg Asn Gln Lys Val Ala Val Ile Gly Gly Gly Asn Thr Ala Val Glu gag gcg ttg tat ctg tct aac atc gct tcg gaa gtg cat ctg att cac 528 Glu Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Ile His cgc cgt gac ggt ttc cgc gcg gaa aaa atc ctc att aag cgc ctg atg 576 Arg Arg Asp Gly Phe Arg Ala Glu Lys Ile Leu Ile Lys Arg Leu Met 185 1.80 gat aaa gtg gag aac ggc aac atc att ctg cac acc aac cgt acg ctg 624 Asp Lys Val Glu Asn Gly Asn Ile Ile Leu His Thr Asn Arg Thr Leu 672 gaa gaa gtg acc ggc gat caa atg ggt gtc act ggc gtt cgt ctg cgc Glu Glu Val Thr Gly Asp Gln Met Gly Val Thr Gly Val Arg Leu Arg 210 gat acg caa aac agc gat aac atc gag tca ctc gac gtt gcc ggt ctg Asp Thr Gln Asn Ser Asp Asn Ile Glu Ser Leu Asp Val Ala Gly Leu 230 235 768 ttt gtt gct atc ggt cac agc ccg aat act gcg att ttc gaa ggg cag Phe Val Ala Ile Gly His Ser Pro Asn Thr Ala Ile Phe Glu Gly Gln

250 255 245 ctg gaa ctg gaa aac ggc tac atc aaa gta cag tcg ggt att cat ggt Leu Glu Leu Glu Asn Gly Tyr Ile Lys Val Gln Ser Gly Ile His Gly 260 265 aat gcc acc cag acc agc att cct ggc gtc ttt gcc gca ggc gac gtg 864 Asn Ala Thr Gln Thr Ser Ile Pro Gly Val Phe Ala Ala Gly Asp Val 280 atg gat cac att tat cgc cag gcc att act tcg gcc ggt aca ggc tgc 912 Met Asp His Ile Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys 295 300 atg gca gca ctt gat gcg gaa cgc tac ctc gat ggt tta gct gac gca 960 Met Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Gly Leu Ala Asp Ala 310 315 aaa taa 966

<210> 45 <211> 321 <212> PRT <213> E. coli

Lys \*

<400> 45 Met Gly Thr Thr Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro 20 Val Leu Ile Thr Gly Met Glu Lys Gly Gly Gln Leu Thr Thr Thr Thr 40 45 35 Glu Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu 55 60 Leu Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile 70 75 Ile Phe Asp His Ile Asn Lys Val Asp Leu Gln Asn Arg Pro Phe Arg Leu Asn Gly Asp Asn Gly Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ala 105 100 Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe 120 125 Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 135 Arg Asn Gln Lys Val Ala Val Ile Gly Gly Gly Asn Thr Ala Val Glu 150 155 Glu Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Ile His 170 165 1.75 Arg Arg Asp Gly Phe Arg Ala Glu Lys Ile Leu Ile Lys Arg Leu Met 180 185 190 Asp Lys Val Glu Asn Gly Asn Ile Ile Leu His Thr Asn Arg Thr Leu 200 Glu Glu Val Thr Gly Asp Gln Met Gly Val Thr Gly Val Arg Leu Arg 220 215 Asp Thr Gln Asn Ser Asp Asn Ile Glu Ser Leu Asp Val Ala Gly Leu 230 235 240 Phe Val Ala Ile Gly His Ser Pro Asn Thr Ala Ile Phe Glu Gly Gln 245 250 Leu Glu Leu Glu Asn Gly Tyr Ile Lys Val Gln Ser Gly Ile His Gly 265 260 Asn Ala Thr Gln Thr Ser Ile Pro Gly Val Phe Ala Ala Gly Asp Val

275 280 285 Met Asp His Ile Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys

295

Met Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Gly Leu Ala Asp Ala

Lys <210> 46 <211> 318 <212> DNA <213> Homo Sapien <220> <221> CDS <222> (1) ... (318) <400> 46 atg gtg aag cag atc gag agc aag act gct ttt cag gaa gcc ttg gac Met Val Lys Gln Ile Glu Ser Lys Thr Ala Phe Gln Glu Ala Leu Asp 48 get gea ggt gat aaa ett gta gta gtt gae tte tea gee aeg tgg tgt 96 Ala Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys 20 ggg cct tgc aaa atg atc aag cct ttc ttt cat tcc ctc tct gaa aag 144 Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys tat tcc aac gtg ata ttc ctt gaa gta gat gtg gat gac tgt cag gat Tyr Ser Asn Val Ile Phe Leu Glu Val Asp Val Asp Cys Gln Asp 192 gtt gct tca gag tgt gaa gtc aaa tgc atg cca aca ttc cag ttt ttt Val Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe 240 288 aag aag gga caa aag gtg ggt gaa ttt tot gga gcc aat aag gaa aag Lys Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys 85 318 ctt gaa gcc acc att aat gaa tta gtc taa Leu Glu Ala Thr Ile Asn Glu Leu Val 100 <210> 47 <211> 105 <212> PRT <213> Homo Sapien <400> 47 Met Val Lys Gln Ile Glu Ser Lys Thr Ala Phe Gln Glu Ala Leu Asp 10 Ala Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys 20 25 Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys 35 40 Tyr Ser Asn Val Ile Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp 55 Val Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe 75 70 Lys Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys 90 Leu Glu Ala Thr Ile Asn Glu Leu Val 100

<210> 48 <211> 1494 <212> DNA <213> Homo sapien <220> <221> CDS <222> (1) ... (1494) <400> 48 atg aac ggc cct gaa gat ctt ccc aag tcc tat gac tat gac ctt atc Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile atc att gga ggt ggc tca gga ggt ctg gca gct gct aag gag cca gcc 96 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Lys Glu Pro Ala 25 caa tat ggc aag aag gtg atg gtc ctg gac ttt ggc act ccc acc cct Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Gly Thr Pro Thr Pro ctt gga act aga tgg ggt ctt gga gga aca tgt gtg aat gtg ggt tgc 192 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys ata cct aaa aaa ctg atg cat caa gca gct ttg tta gga caa gcc ctg 240 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 caa gac tct cga aat tat gga tgg aaa gtc gag gag aca gtt aag cat 288 Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His gat tgg gac aga atg ata gaa gct gta cag aat cac att ggc tct ttg 336 Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 105 aat tgg ggc tac cga gta gct ctg cgg gag aaa aaa gtc gtc tat gag Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 384 120 aat gct tat ggg caa ttt att ggt cct cac agg att aag gca aca aat 432 1 Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn 130 135 aat aaa ggc aaa gaa aaa att tat tca gca gag aga ttt ctc att gcc Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala 145 act ggt gaa aga cca cgt tac ttg ggc atc cct ggt gac aaa gaa tac 528 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr tgc atc agc agt gat gat ctt ttc tcc ttg cct tac tgc ccg ggt aag 576 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 180 185 aca ctg gtt gtt gga gca tcc tat gtc gct ttg gag tgc gct gga ttt 624 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 200 ctt gct ggt att ggt tta gac gtc act gtt atg gtt agg tcc att ctt 672 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu ctt aga gga ttt gac cag gac atg gcc aac aaa att ggt gaa cac atg 720

| Leu<br>225        | Arg               | Gly               | Phe               | Asp        | Gln<br>230        | Asp               | Met               | Ala               | Asn        | Lys<br>235        | Ile               | Gly               | Glu               | His        | Met<br>240        |      |
|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|------|
|                   |                   |                   |                   |            | aag<br>Lys        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 768  |
| gaa<br>Glu        | caa<br>Gln        | att<br>Ile        | gaa<br>Glu<br>260 | gca<br>Ala | gjå<br>aaa        | aca<br>Thr        | cca<br>Pro        | ggc<br>Gly<br>265 | cga<br>Arg | ctc<br>Leu        | aga<br>Arg        | gta<br>Val        | gta<br>Val<br>270 | gct<br>Ala | cag<br>Gln        | 816  |
| tcc<br>Ser        | acc<br>Thr        | aat<br>Asn<br>275 | agt<br>Ser        | gag<br>Glu | gaa<br>Glu        | atc<br>Ile        | att<br>Ile<br>280 | gaa<br>Glu        | gga<br>Gly | gaa<br>Glu        | tat<br>Tyr        | aat<br>Asn<br>285 | acg<br>Thr        | gtg<br>Val | atg<br>Met        | 864  |
| ctg<br>Leu        | gca<br>Ala<br>290 | ata<br>Ile        | gga<br>Gly        | aga<br>Arg | gat<br>Asp        | gct<br>Ala<br>295 | tgc<br>Cys        | aca<br>Thr        | aga<br>Arg | aaa<br>Lys        | att<br>Ile<br>300 | ggc               | tta<br>Leu        | gaa<br>Glu | acc<br>Thr        | 912  |
|                   |                   |                   |                   |            | aat<br>Asn<br>310 |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 960  |
|                   |                   |                   |                   |            | gtg<br>Val        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1008 |
|                   |                   |                   |                   |            | ctc<br>Leu        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1056 |
|                   |                   |                   |                   |            | tat<br>Tyr        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1104 |
|                   |                   |                   |                   |            | gta<br>Val        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1152 |
| ctt<br>Leu<br>385 | tct<br>Ser        | gag<br>Glu        | gag<br>Glu        | aaa<br>Lys | gct<br>Ala<br>390 | gtg<br>Val        | gag<br>Glu        | aag<br>Lys        | ttt<br>Phe | 395<br>995        | gaa<br>Glu        | gaa<br>Glu        | aat<br>Asn        | att<br>Ile | gag<br>Glu<br>400 | 1200 |
|                   |                   |                   |                   |            | ttt<br>Phe        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1248 |
|                   |                   |                   |                   |            | tat<br>Tyr        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1296 |
|                   |                   |                   |                   |            | ttt<br>Phe        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1344 |
| aca<br>Thr        | caa<br>Gln<br>450 | ggc<br>Gly        | ttt<br>Phe        | gca<br>Ala | gct<br>Ala        | gcg<br>Ala<br>455 | ctc<br>Leu        | aaa<br>Lys        | tgt<br>Cys | gga<br>Gly        | ctg<br>Leu<br>460 | acc<br>Thr        | aaa,<br>Lys       | aag<br>Lys | cag<br>Gln        | 1392 |
| ctg<br>Leu<br>465 | gac<br>Asp        | agc<br>Ser        | aca<br>Thr        | att<br>Ile | gga<br>Gly<br>470 | atc<br>Ile        | cac<br>His        | cct<br>Pro        | gtc<br>Val | tgt<br>Cys<br>475 | gca<br>Ala        | gag<br>Glu        | gta<br>Val        | ttc<br>Phe | aca<br>Thr<br>480 | 1440 |
|                   |                   |                   |                   |            | aag<br>Lys        |                   |                   |                   |            |                   |                   |                   |                   |            |                   | 1488 |

tgc tga 1494 Cys \*

<210> 49 <211> 497 <212> PRT <213> Homo sapien

<400> 49 Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Pro Ala 20 25 Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Gly Thr Pro Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 105 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 115 120 125 Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn 135 140 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala 150 155 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 165 170 175 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 180 185 190 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 200 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 215 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 230 235 Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val 245 250 255 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln 265 Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met 280 Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr 295 300 Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp 310 315 Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu 325 330 Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu 345 350 Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu 360 365 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly 375 380 Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu 390 395 Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg 405 410 Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn 420 425 430 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val

Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln
450

Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr
465

Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly
485

Cys

<210> 50 <211> 1377 <212> DNA <213> Mycobacterium leprae <220> <221> CDS <222> (1)...(1377) atg aac acc act cct tct geg cat gag acg ata cac gaa gtg atc gtt 48 Met Asn Thr Thr Pro Ser Ala His Glu Thr Ile His Glu Val Ile Val att ggc tcc ggt cca gca ggc tac act gct gcc ctg tac gcc gct cgt Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Ala Ala Arg 96 gca cag cta aca ccg ctg gta ttt gag ggt acc tca ttc ggc ggc gcg 144 Ala Gln Leu Thr Pro Leu Val Phe Glu Gly Thr Ser Phe Gly Gly Ala ctg atg acc acc gag gtg gaa aac tac cca ggt ttt cgc aac ggc 192 Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly ata acc ggc ccg gag ttg atg gac gat atg cgt gaa cag gca ctg cga Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg 240 ttc ggc gcg gaa ctg cgg acc gaa gac gtc gag tcg gta tca ttg cgt 288 Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg 90 ggc ccg atc aaa tcg gtc gtc acc gct gaa gga cag act tat cag gcc 336 Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala cga gcc gtc atc ctc gcc atg ggt acc tcc gtg cgt tat cta cag atc 384 Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile ccc ggc gag caa gaa ttg cta gga cgt ggc gtg agt gca tgc gcg acc Pro Gly Glu Gln Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr tgc gac ggg tcc ttt ttc cgc ggc caa gac att gcc gtc att ggc ggt 480 Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly 150 gga gac tca gcg atg gag gaa gcc ctc ttt ttg acc cgg ttc gcc cgc 528 Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg 170 age gtc acg ctc gtg cac cgc cgc gac gaa ttc cga gct tct aag atc Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile

| atg<br>Met | ctc<br>Leu        | ggt<br>Gly<br>195 | cgc<br>Arg | gcc<br>Ala        | cgt<br>Arg        | aac<br>Asn        | aat<br>Asn<br>200 | gac<br>Asp | aag<br>Lys        | atc<br>Ile | aaa<br>Lys        | ttc<br>Phe<br>205 | atc<br>Ile | acc<br>Thr        | aac<br>Asn | 624  |
|------------|-------------------|-------------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|------------|-------------------|-------------------|------------|-------------------|------------|------|
| cac<br>His | acc<br>Thr<br>210 | gtg<br>Val        | gtc<br>Val | gcg<br>Ala        | gtg<br>Val        | aac<br>Asn<br>215 | Gly<br>aaa        | tat<br>Tyr | aca<br>Thr        | aca<br>Thr | gtg<br>Val<br>220 | acc<br>Thr        | gga<br>Gly | ttg<br>Leu        | cgg<br>Arg | 672  |
|            |                   |                   |            |                   | acg<br>Thr<br>230 |                   |                   |            |                   |            |                   |                   |            |                   |            | 720  |
|            |                   |                   |            |                   | Gly               |                   |                   |            |                   |            |                   |                   |            |                   |            | 768  |
|            |                   |                   |            |                   | ccg<br>Pro        |                   |                   |            |                   |            |                   |                   |            |                   |            | 816  |
|            |                   |                   |            |                   | gac<br>Asp        |                   |                   |            |                   |            |                   |                   |            |                   |            | 864  |
| cgc<br>Arg | acc<br>Thr<br>290 | tac<br>Tyr        | cgg<br>Arg | cag<br>Gln        | gcg<br>Ala        | atc<br>Ile<br>295 | act<br>Thr        | gcc<br>Ala | gca<br>Ala        | ggt<br>Gly | agt<br>Ser<br>300 | ggc<br>Gly        | tgt<br>Cys | gcc<br>Ala        | gcc<br>Ala | 912  |
|            |                   |                   |            |                   | cgt<br>Arg<br>310 |                   |                   |            |                   |            |                   |                   |            |                   |            | 960  |
| aac<br>Asn | gaa<br>Glu        | aca<br>Thr        | aca<br>Thr | gag<br>Glu<br>325 | gaa<br>Glu        | act<br>Thr        | gga<br>Gly        | gac<br>Asp | gtt<br>Val<br>330 | gac<br>Asp | agt<br>Ser        | acc<br>Thr        | gac<br>Asp | aca<br>Thr<br>335 | acc<br>Thr | 1008 |
|            |                   |                   |            |                   | atg<br>Met        |                   |                   |            |                   |            |                   |                   |            |                   |            | 1056 |
|            |                   |                   |            |                   | tcc<br>Ser        |                   |                   |            |                   |            |                   |                   |            |                   |            | 1104 |
|            |                   |                   |            |                   | ttt<br>Phe        |                   |                   |            |                   |            |                   |                   |            |                   |            | 1152 |
|            |                   |                   |            |                   | gaa<br>Glu<br>390 |                   |                   |            |                   |            |                   |                   |            |                   |            | 1200 |
| act<br>Thr | gtc<br>Val        | gcc<br>Ala        | aag<br>Lys | tta<br>Leu<br>405 | gat<br>Asp        | gta<br>Val        | gac<br>Asp        | acc<br>Thr | aac<br>Asn<br>410 | ccg<br>Pro | gaa<br>Glu        | atg<br>Met        | gca<br>Ala | cgc<br>Arg<br>415 | gag<br>Glu | 1248 |
|            |                   |                   |            |                   | ata<br>Ile        |                   |                   |            |                   |            |                   |                   |            |                   |            | 1296 |
| cca<br>Pro | gta<br>Val        | aaa<br>Lys<br>435 | cgc<br>Arg | atc<br>Ile        | gtt<br>Val        | gly<br>ggc        | gct<br>Ala<br>440 | aag<br>Lys | ggc<br>Gly        | aaa<br>Lys | gca<br>Ala        | gcg<br>Ala<br>445 | tta<br>Leu | cta<br>Leu        | cgt<br>Arg | 1344 |
| gac<br>Asp | ctt<br>Leu        | tcc<br>Ser        | gac<br>Asp | gtg<br>Val        | gta<br>Val        | ect<br>Pro        | aac<br>Asn        | ctc<br>Leu | aat<br>Asn        | tag<br>*   |                   |                   |            |                   |            | 1377 |

450 455

<210> 51 <211> 458 <212> PRT <213> Mycobacterium leprae

Met Asn Thr Thr Pro Ser Ala His Glu Thr Ile His Glu Val Ile Val 10 Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Ala Ala Arg 20 25 Ala Gln Leu Thr Pro Leu Val Phe Glu Gly Thr Ser Phe Gly Gly Ala Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly 55 Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala 100 105 Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile 120 125 Pro Gly Glu Gln Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr 135 140 Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly 150 155 Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg 170 165 1.75 Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile 180 185 Met Leu Gly Arg Ala Arg Asn Asn Asp Lys Ile Lys Phe Ile Thr Asn 195 200 His Thr Val Val Ala Val Asn Gly Tyr Thr Thr Val Thr Gly Leu Arg 215 220 Leu Arg Asn Thr Thr Gly Glu Glu Thr Thr Leu Val Val Thr Gly 235 230 Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Ser Leu Val Ser Asp 245 250 Val Val Asp Ile Asp Pro Asp Gly Tyr Val Leu Val Lys Gly Arg Thr 265 Thr Ser Thr Ser Met Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp 285 280 Arg Thr Tyr Arg Gln Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala 295 Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Gly Ser Lys Ala 315 Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr Thr 330 325 335 Asp Trp Ser Thr Ala Met Thr Asp Ala Lys Asn Ala Gly Val Thr Ile 340 345 350 Glu Val Thr Asp Ala Ser Phe Phe Ala Asp Val Leu Ser Ser Asn Lys 360 365 Pro Val Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Lys Met 375 380 Val Ala Pro Val Leu Glu Glu Ile Ala Ser Glu Gln Arg Asn Gln Leu . 390 395 Thr Val Ala Lys Leu Asp Val Asp Thr Asn Pro Glu Met Ala Arg Glu 405 410 Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gln 425 Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg 435 440 Asp Leu Ser Asp Val Val Pro Asn Leu Asn

```
<210> 52
<211> 178
<212> PRT
<213> Arabidopsis thaliana
<400> 52
Met Pro Leu Ser Leu Arg Leu Ser Pro Ser Pro Thr Ala Leu Ser Pro
                                    10
Thr Thr Gly Gly Phe Gly Pro Ser Arg Lys Gln Cys Arg Ile Pro Tyr
           20
                                25
Ser Gly Val Pro Thr Thr Lys Ile Gly Phe Cys Ser Leu Asp Ser Arg
                            40
Lys Arg Gly Asp Ser Ser Val Val Arg Cys Ser Leu Glu Thr Val Asn
                        55
Val Ser Val Gly Gln Val Thr Glu Val Asp Lys Asp Thr Phe Trp Pro
                    70
Ile Val Lys Ala Ala Gly Glu Lys Leu Val Val Leu Asp Met Tyr Thr
                                    90
Gln Trp Cys Gly Pro Cys Lys Val Ile Ala Pro Lys Tyr Lys Ala Leu
           100
                                105
Ser Glu Lys Tyr Asp Asp Val Val Phe Leu Lys Leu Asp Cys Asn Pro
       115
                            120
Asp Asn Arg Pro Leu Pro Lys Glu Leu Gly Ile Arg Val Val Pro Thr
                        135
Phe Lys Ile Leu Lys Asp Asn Lys Val Val Lys Glu Val Thr Gly Ala
                                        155
                    150
Lys Tyr Asp Asp Leu Val Ala Ala Ile Glu Thr Ala Arg Ser Ala Ala
Ser Gly
<210> 53
<211> 185
<212> PRT
<213> Arabidopsis thaliana
```

Met Pro Leu Ser Leu Arg Leu Ala Pro Ser Pro Thr Ser Phe Arg Tyr 10 Ser Pro Ile Thr Ser Thr Gly Ala Gly Gly Phe Ser Pro Val Lys Gln His Cys Arg Ile Pro Asn Ser Gly Val Ala Thr Lys Ile Gly Phe Cys 40 Ser Gly Gly Gly Val Leu Asp Ser Gly Arg Arg Ile Gly Ser Cys 55 Val Val Arg Cys Ser Leu Glu Thr Val Asn Val Thr Val Gly Gln Val 70 Thr Glu Val Asp Lys Asp Thr Phe Trp Pro Ile Val Lys Ala Ala Gly 85 90 Asp Lys Ile Val Val Leu Asp Met Tyr Thr Gln Trp Cys Gly Pro Cys 105 Lys Val Ile Ala Pro Lys Tyr Lys Glu Leu Ser Glu Lys Tyr Gln Asp 120 125 115 Met Val Phe Leu Lys Leu Asp Cys Asn Gln Asp Asn Lys Pro Leu Ala 140 135 Lys Glu Leu Gly Ile Arg Val Val Pro Thr Phe Lys Ile Leu Lys Asp 150 155 Asn Lys Val Val Lys Glu Val Thr Gly Ala Lys Tyr Glu Asp Leu Leu 165 170 Ala Ala Ile Glu Ala Ala Arg Ser Gly 180

<210> 54 <211> 182

<212> PRT <213> Brassica napus

<400> 54 Met Pro Leu Ser Leu Arg Leu Ala Pro Ser Pro Thr Ala Leu Ser Pro Thr Thr Gly Gly Phe Ser Pro Ala Lys Lys Gln Cys Arg Ile Pro Ser 25 Tyr Ser Gly Val Ala Thr Thr Thr Arg Arg Ile Gly Leu Cys Ser Leu Asp Tyr Val Lys Arg Gly Asp Ser Ser Val Val Arg Cys Ser Leu Gln 55 Thr Val Asn Val Ser Val Gly Gln Val Thr Glu Val Asp Lys Asp Thr 70 75 Phe Trp Pro Ile Val Lys Ala Ala Gly Glu Lys Ile Val Val Leu Asp 85 90 Met Tyr Thr Gln Trp Cys Gly Pro Cys Lys Val Ile Ala Pro Lys Tyr 105 Lys Ala Leu Ser Glu Lys Tyr Glu Asp Val Val Phe Leu Lys Leu Asp 120 115 125 Cys Asn Pro Glu Asn Arg Pro Leu Ala Lys Glu Leu Gly Ile Arg Val 135 Val Pro Thr Phe Lys Ile Leu Lys Asp Asn Gln Val Val Lys Glu Val 150 155 Thr Gly Ala Lys Tyr Asp Asp Leu Val Ala Ala Ile Glu Thr Ala Arg 165 170 Ser Ala Ser Ser Ser Gly 180

<210> 55 <211> 191 <212> PRT

<213> Mesembryanthemum crystallinum

<400> 55 Met Ala Met Gln Leu Ser Leu Ser His Gln Ser Trp Ala Lys Ser Leu Ala Ser Pro Ile Thr Ser Phe Asp Pro Ala Arg Ser Pro Pro Lys Arg 20 25 Val Glu Leu Gly Pro Asn Cys Leu Asn Gly Gly Ala Thr Ala Gly Lys 40 45 Leu Met Arg Glu Lys Val Gly Glu Arg Met Arg Met Ser Gly Arg Ser 55 Cys Cys Val Lys Ala Ser Leu Glu Thr Ala Val Gly Ala Glu Ser Glu Thr Leu Val Gly Lys Val Thr Glu Val Asp Lys Asp Thr Phe Trp Pro 85 90 Ile Ala Asn Gly Ala Gly Asp Lys Pro Val Val Leu Asp Met Tyr Thr 100 105 Gln Trp Cys Gly Pro Cys Lys Val Met Ala Pro Lys Tyr Gln Glu Leu 115 120 Ala Glu Lys Leu Leu Asp Val Val Phe Leu Lys Leu Asp Cys Asn Gln 135 140 Glu Asn Lys Pro Leu Ala Lys Glu Leu Gly Ile Arg Val Val Pro Thr 150 155 Phe Lys Ile Leu Lys Gly Gly Lys Ile Val Asp Glu Val Thr Gly Ala 165 170 Lys Phe Asp Lys Leu Val Ala Ala Ile Glu Ala Ala Arg Ser Ser 180

<210> 56 <211> 182 <212> PRT <213> Pisum sativum

<400> 56 Met Ala Leu Asn Leu Cys Thr Ser Pro Lys Trp Ile Gly Thr Thr Val 10 Phe Asp Ser Ala Ser Ser Ser Lys Pro Ser Leu Ala Ser Ser Phe Ser 20 25 Thr Thr Ser Phe Ser Ser Ser Ile Leu Cys Ser Lys Arg Val Gly Leu 35 40 45 Gln Arg Leu Ser Leu Arg Arg Ser Ile Ser Val Ser Val Arg Ser Ser Leu Glu Thr Ala Gly Pro Thr Val Thr Val Gly Lys Val Thr Glu Val 70 75 Asn Lys Asp Thr Phe Trp Pro Ile Val Asn Ala Ala Gly Asp Lys Thr 95 85 90 Val Val Leu Asp Met Phe Thr Lys Trp Cys Gly Pro Cys Lys Val Ile 100 105 110 Ala Pro Leu Tyr Glu Glu Leu Ser Gln Lys Tyr Leu Asp Val Val Phe 125 120 Leu Lys Leu Asp Cys Asn Gln Asp Asn Lys Ser Leu Ala Lys Glu Leu 130 135 140 Gly Ile Lys Val Val Pro Thr Phe Lys Ile Leu Lys Asp Asn Lys Ile 150 155 Val Lys Glu Val Thr Gly Ala Lys Phe Asp Asp Leu Val Ala Ala Ile 165 170 Asp Thr Val Arg Ser Ser 180

<210> 57 <211> 190 <212> PRT <213> Spinacia oleracea

<400> 57 Met Ala Leu His Leu Ser Leu Ser His Gln Ser Trp Thr Ser Pro Ala His Pro Ile Thr Ser Ser Asp Pro Thr Arg Ser Ser Val Pro Gly Thr 25 Gly Leu Ser Arg Arg Val Asp Phe Leu Gly Ser Cys Lys Ile Asn Gly 35 40 Val Phe Val Val Lys Arg Lys Asp Arg Arg Arg Met Arg Gly Glu 55 Val Arg Ala Ser Met Glu Gln Ala Leu Gly Thr Gln Glu Met Glu Ala Ile Val Gly Lys Val Thr Glu Val Asn Lys Asp Thr Phe Trp Pro Ile 85 90 Val Lys Ala Ala Gly Asp Lys Pro Val Val Leu Asp Met Phe Thr Gln 105 110 Trp Cys Gly Pro Cys Lys Ala Met Ala Pro Lys Tyr Glu Lys Leu Ala 115 120 125 Glu Glu Tyr Leu Asp Val Ile Phe Leu Lys Leu Asp Cys Asn Gln Glu 135 140 Asn Lys Thr Leu Ala Lys Glu Leu Gly Ile Arg Val Val Pro Thr Phe 150 155 Lys Ile Leu Lys Glu Asn Ser Val Val Gly Glu Val Thr Gly Ala Lys 165 170 Tyr Asp Lys Leu Leu Glu Ala Ile Gln Ala Ala Arg Ser Ser,

<210> 58 <211> 106 <212> PRT <213> Anabaena

<400> 58
Ser Ala Ala Gln Val Thr Asp Ser Thr Phe Lys Gln Glu Val Leu
1 5 10 15

Asp Ser Asp Val Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys Arg Met Val Ala Pro Val Val Asp Glu Ile Ala Gln Gln Tyr Glu Gly Lys Ile Lys Val Val Lys Val Asn Thr Asp Glu Asn Pro Gln 55 60 Val Ala Ser Gln Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Ile Phe Lys Gly Gly Gln Lys Val Asp Wet Val Val Gly Ala Val Pro Lys Thr 85 90 Thr Leu Ser Gln Thr Leu Glu Lys His Leu 100

<210> 59 <211> 179 <212> PRT <213> Arabidopsis thaliana

Met Ala Ala Tyr Thr Cys Thr Ser Arg Pro Pro Ile Ser Ile Arg Ser Glu Met Arg Ile Ala Ser Ser Pro Thr Gly Ser Phe Ser Thr Arg Gln 20 25 Met Phe Ser Val Leu Pro Glu Ser Ser Gly Leu Arg Thr Arg Val Ser 35 40 Leu Ser Ser Leu Ser Lys Asn Ser Arg Val Ser Arg Leu Arg Arg Gly 55 Val Ile Cys Glu Ala Gln Asp Thr Ala Thr Gly Ile Pro Val Val Asn 70 75 Asp Ser Thr Trp Asp Ser Leu Val Leu Lys Ala Asp Glu Pro Val Phe 85 90 Val Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys Lys Met Ile Asp Pro 100 105 Ile Val Asn Glu Leu Ala Gln Lys Tyr Ala Gly Gln Phe Lys Phe Tyr 120

130 135 140 Arg Ser Ile Pro Thr Ile Met Ile Phe Val Asn Gly Glu Lys Lys Asp 150 155 Thr Ile Ile Gly Ala Val Ser Lys Asp Thr Leu Ala Thr Ser Ile Asn

Lys Leu Asn Thr Asp Glu Ser Pro Ala Thr Pro Gly Gln Tyr Gly Val

Lys Phe Leu

<400> 59

<210> 60 <211> 186 <212> PRT <213> Arabidopsis thaliana

<400> 60 Met Ala Ala Phe Thr Cys Thr Ser Arg Pro Pro Ile Ser Leu Arg Ser 10 Glu Thr Arg Ile Val Ser Ser Ser Pro Ser Ala Ser Ser Leu Ser Ser Arg Arg Met Phe Ala Val Leu Pro Glu Ser Ser Gly Leu Arg Ile Arg 35 40 45 Leu Ser Leu Ser Pro Ala Ser Leu Thr Ser Ile His Gln Pro Arg Val 55 Ser Arg Leu Arg Arg Ala Val Val Cys Glu Ala Gln Glu Thr Thr 70 Asp Ile Gln Val Val Asn Asp Ser Thr Trp Asp Ser Leu Val Leu Lys 90 85 Ala Thr Gly Pro Val Val Val Asp Phe Trp Ala Pro Trp Cys Gly Pro 100 105 Cys Lys Met Ile Asp Pro Leu Val Asn Asp Leu Ala Gln His Tyr Thr

<210> 61 <211> 173 <212> PRT

<213> Arabidopsis thaliana

<400> 61 Met Ala Ile Ser Ser Ser Ser Ser Ile Cys Phe Asn Pro Thr Arg 10 Phe His Thr Ala Arg His Ile Ser Ser Pro Ser Arg Leu Phe Pro Val 25 Thr Ser Phe Ser Pro Arg Ser Leu Arg Phe Ser Asp Arg Arg Ser Leu 40 45 Leu Ser Ser Ser Ala Ser Arg Leu Arg Leu Ser Pro Leu Cys Val Arg 55 Asp Ser Arg Ala Ala Glu Val Thr Gln Arg Ser Trp Glu Asp Sér Val 70 75 Leu Lys Ser Glu Thr Pro Val Leu Val Glu Phe Tyr Thr Ser Trp Cys 85 90 Gly Pro Cys Arg Met Val His Arg Ile Ile Asp Glu Ile Ala Gly Asp 100 105 Tyr Ala Gly Lys Leu Asn Cys Tyr Leu Leu Asn Ala Asp Asn Asp Leu 115 120 125 Pro Val Ala Glu Glu Tyr Glu Ile Lys Ala Val Pro Val Val Leu Leu 135 140 Phe Lys Asn Gly Glu Lys Arg Glu Ser Ile Met Gly Thr Met Pro Lys 150 155 Glu Phe Tyr Ile Ser Ala Ile Glu Arg Val Leu Asn Ser

<210> 62 <211> 193 <212> PRT

<213> Arabidopsis thaliana

<400> 62 Met Ala Ser Leu Leu Asp Ser Val Thr Val Thr Arg Val Phe Ser Leu Pro Ile Ala Ala Ser Val Ser Ser Ser Ser Ala Ala Pro Ser Val Ser Arg Arg Ile Ser Pro Ala Arg Phe Leu Glu Phe Arg Gly Leu Lys 40 Ser Ser Arg Ser Leu Val Thr Gln Ser Ala Ser Leu Gly Ala Asn Arg 55 Arg Thr Arg Ile Ala Arg Gly Gly Arg Ile Ala Cys Glu Ala Gln Asp Thr Thr Ala Ala Ala Val Glu Val Pro Asn Leu Ser Asp Ser Glu Trp 90 85 Gln Thr Lys Val Leu Glu Ser Asp Val Pro Val Leu Val Glu Phe Trp 100 105 Ala Pro Trp Cys Gly Pro Cys Arg Met Ile His Pro Ile Val Asp Gln 115 120 Leu Ala Lys Asp Phe Ala Gly Lys Phe Lys Phe Tyr Lys Ile Asn Thr 135 140 Asp Glu Ser Pro Asn Thr Pro Asn Arg Tyr Gly Ile Arg Ser Val Pro 155

Thr Val Ile Ile Phe Lys Gly Gly Glu Lys Lys Asp Ser Ile Ile Gly 165 170 175

Ala Val Pro Arg Glu Thr Leu Glu Lys Thr Ile Glu Arg Phe Leu Val 180 185 190

Glu

<210> 63. <211> 177 <212> PRT <213> Brassica napus

<400> 63 Met Ala Ala Phe Thr Cys Thr Ser Ser Pro Pro Ile Ser Leu Arg Ser 10 Glu Met Met Ile Ala Ser Ser Lys Thr Val Ser Leu Ser Thr Arg Gln 25 Met Phe Ser Val Gly Gly Leu Arg Thr Arg Val Ser Leu Ser Ser Val 35 40 Ser Lys Asn Ser Arg Ala Ser Arg Leu Arg Arg Gly Gly Ile Ile Cys 55 Glu Ala Gln Asp Thr Ala Thr Gly Ile Pro Met Val Asn Asp Ser Thr 75 Trp Glu Ser Leu Val Leu Lys Ala Asp Glu Pro Val Val Val Asp Phe 85 90 95 Trp Ala Pro Trp Cys Gly Pro Cys Lys Met Ile Asp Pro Ile Val Asn 100 105 Glu Leu Ala Gln Gln Tyr Thr Gly Lys Ile Lys Phe Phe Lys Leu Asn 120 Thr Asp Asp Ser Pro Ala Thr Pro Gly Lys Tyr Gly Val Arg Ser Ile 130 135 140 Pro Thr Ile Met Ile Phe Val Lys Gly Glu Lys Lys Asp Thr Ile Ile 150 155 Gly Ala Val Pro Lys Thr Thr Leu Ala Thr Ser Ile Asp Lys Phe Leu

<210> 64 <211> 140 <212> PRT <213> Chlamydomonas reinhardtii

Met Ala Leu Val Ala Arg Arg Ala Ala Val Pro Ser Ala Arg Ser Ser 10 Ala Arg Pro Ala Phe Ala Arg Ala Pro Arg Arg Ser Val Val Arg Ala Glu Ala Gly Ala Val Asn Asp Asp Thr Phe Lys Asn Val Val 40 Leu Glu Ser Ser Val Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys 55 60 Gly Pro Cys Arg Ile Ile Ala Pro Val Val Asp Glu Ile Ala Gly Glu 75 Tyr Lys Asp Lys Leu Lys Cys Val Lys Leu Asn Thr Asp Glu Ser Pro 90 Asn Val Ala Ser Glu Tyr Gly Ile Arg Ser Ile Pro Thr Ile Met Val 105 Phe Lys Gly Gly Lys Lys Cys Glu Thr Ile Ile Gly Ala Val Pro Lys 120 Ala Thr Ile Val Gln Thr Val Glu Lys Tyr Leu Asn

<210> 65

Gln

<211> 167 <212> PRT <213> Zea mays

<400> 65 Met Ala Met Glu Thr Cys Phe Arg Ala Trp Ala Leu His Ala Pro Ala Gly Ser Lys Asp Arg Leu Leu Val Gly Asn Leu Val Leu Pro Ser Lys 20 Arg Ala Leu Ala Pro Leu Ser Val Gly Arg Val Ala Thr Arg Arg Pro 40 Arg His Val Cys Gln Ser Lys Asn Ala Val Asp Glu Val Val Val Ala 55 Asp Glu Lys Asn Trp Asp Gly Leu Val Met Ala Cys Glu Thr Pro Val 70 . Leu Val Glu Phe Trp Ala Pro Trp Cys Gly Pro Cys Arg Met Ile Ala 85 90 Pro Val Ile Asp Glu Leu Ala Lys Asp Tyr Ala Gly Lys Ile Thr Cys 105 100 Cys Lys Val Asn Thr Asp Asp Ser Pro Asn Val Ala Ser Thr Tyr Gly 125 120 115 Ile Arg Ser Ile Pro Thr Val Leu Ile Phe Lys Gly Gly Glu Lys Lys 135 140 Glu Ser Val Ile Gly Ala Val Pro Lys Ser Thr Leu Thr Thr Leu Ile 150 155 145 Asp Lys Tyr Ile Gly Ser Ser 165

<210> 66 <211> 172 <212> PRT <213> Oryza sativa

<400> 66 Met Ala Leu Glu Thr Cys Phe Arg Ala Trp Ala Thr Leu His Ala Pro 10 Gln Pro Pro Ser Ser Gly Gly Ser Arg Asp Arg Leu Leu Leu Ser Gly Ala Gly Ser Ser Gln Ser Lys Pro Arg Leu Ser Val Ala Ser Pro Ser 40 Pro Leu Arg Pro Ala Ser Arg Phe Ala Cys Gln Cys Ser Asn Val Val 60 55 Asp Glu Val Val Val Ala Asp Glu Lys Asn Trp Asp Ser Met Val Leu 70 75 Gly Ser Glu Ala Pro Val Leu Val Glu Phe Trp Ala Pro Trp Cys Gly 95 85 Pro Cys Arg Met Ile Ala Pro Val Ile Asp Glu Leu Ala Lys Glu Tyr 105 110 Val Gly Lys Ile Lys Cys Cys Lys Val Asn Thr Asp Asp Ser Pro Asn 115 120 125 Ile Ala Thr Asn Tyr Gly Ile Arg Ser Ile Pro Thr Val Leu Met Phe 135 140 Lys Asn Gly Glu Lys Lys Glu Ser Val Ile Gly Ala Val Pro Lys Thr 150 155 Thr Leu Ala Thr Ile Ile Asp Lys Tyr Val Ser Ser

<210> 67 <211> 172 <212> PRT <213> Pisum sativum

165

Ser Ser Ser Ile Val Phe Ile Phe Lys Gly Lys Ala Cys Leu Leu Thr 25 Ser Lys Ser Arg Ile Gln Glu Ser Phe Ala Glu Leu Asn Ser Phe Thr Ser Leu Val Leu Leu Ile Glu Asn His Val Leu Leu His Ala Arg Glu 55 Ala Val Asn Glu Val Gln Val Val Asn Asp Ser Ser Trp Asp Glu Leu Val Ile Gly Ser Glu Thr Pro Val Leu Val Asp Phe Trp Ala Pro Trp 90 Cys Gly Pro Cys Arg Met Ile Ala Pro Ile Ile Asp Glu Leu Ala Lys 100 105 Glu Tyr Ala Gly Lys Ile Lys Cys Tyr Lys Leu Asn Thr Asp Glu Ser 115 120 125 Pro Asn Thr Ala Thr Lys Tyr Gly Ile Arg Ser Ile Pro Thr Val Leu 135 140 Phe Phe Lys Asn Gly Glu Arg Lys Asp Ser Val Ile Gly Ala Val Pro 150 155 Lys Ala Thr Leu Ser Glu Lys Val Glu Lys Tyr Ile

<210> 68 <211> 181 <212> PRT <213> Spinacia oleracea

<400> 68 Met Ala Ile Glu Asn Cys Leu Gln Leu Ser Thr Ser Ala Ser Val Gly 10 Thr Val Ala Val Lys Ser His Val His His Leu Gln Pro Ser Ser Lys 25 Val Asn Val Pro Thr Phe Arg Gly Leu Lys Arg Ser Phe Pro Ala Leu 40 Ser Ser Ser Val Ser Ser Ser Pro Arg Gln Phe Arg Tyr Ser Ser 55 Val Val Cys Lys Ala Ser Glu Ala Val Lys Glu Val Gln Asp Val Asn 70 75 Asp Ser Ser Trp Lys Glu Phe Val Leu Glu Ser Glu Val Pro Val Met 85 90 Val Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys Lys Leu Ile Ala Pro 100 105 Val Ile Asp Glu Leu Ala Lys Glu Tyr Ser Gly Lys Ile Ala Val Tyr 115 120 125 Lys Leu Asn Thr Asp Glu Ala Pro Gly Ile Ala Thr Gln Tyr Asn Ile 135 140 Arg Ser Ile Pro Thr Val Leu Phe Phe Lys Asn Gly Glu Arg Lys Glu 150 155 Ser Ile Ile Gly Ala Val Pro Lys Ser Thr Leu Thr Asp Ser Ile Glu 165 Lys Tyr Leu Ser Pro

<210> 69 <211> 175 <212> PRT <213> Triticum aestivum

180

```
55
Asn Val Val Asp Glu Val Ile Val Ala Asp Glu Lys Asn Trp Asp Asn
Met Val Ile Ala Cys Glu Ser Pro Val Leu Val Glu Phe Trp Ala Pro
                85
                                   90
Trp Cys Gly Pro Cys Arg Met Ile Ala Pro Val Ile Asp Glu Leu Ala
           100
                               105
Lys Asp Tyr Val Gly Lys Ile Lys Cys Cys Lys Val Asn Thr Asp Asp
                            120
Cys Pro Asn Ile Ala Ser Thr Tyr Gly Ile Arg Ser Ile Pro Thr Val
                       135
Leu Met Phe Lys Asp Gly Glu Lys Lys Glu Ser Val Ile Gly Ala Val
                   150
                                       155
Pro Lys Thr Thr Leu Cys Thr Ile Ile Asp Lys Tyr Ile Gly Ser
```

<210> 70

<211> 106

<212> PRT

<213> Anacystis nidulans

<400> 70 Ser Val Ala Ala Ala Val Thr Asp Ala Thr Phe Lys Gln Glu Val Leu 1 10 Glu Ser Ser Ile Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly 25 Pro Cys Arg Met Val Ala Pro Val Val Asp Glu Ile Ala Gln Gln Tyr 40 35 Ser Asp Gln Val Lys Val Lys Val Asn Thr Asp Glu Asn Pro Ser 55 60 Val Ala Ser Gln Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Ile Phe 70 Lys Asp Gly Gln Arg Val Asp Thr Val Val Gly Ala Val Pro Lys Thr 85 90 Thr Leu Ala Asn Thr Leu Asp Lys His Leu

100 105

<210> 71

<211> 107

<212> PRT

<213> Cyanidium caldarium

Ser Thr Leu Thr Asn Ala Leu Lys Lys Tyr Leu 100 105

<210> 72

<211> 102

<212> PRT

<213> Cyanidioschyzon merolae

<400> 72

Met Leu His Ile Asp Glu Leu Thr Phe Glu Asn Glu Val Leu Gln Ser 10 Glu Lys Leu Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys 25 Arg Met Ile Gly Pro Ile Leu Glu Glu Ile Ala Lys Glu Phe Asn Leu 40 Lys Val Val Gln Val Asn Thr Asp Glu Asn Pro Asn Leu Ala Thr Phe 55 60 Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Leu Phe Lys Lys Gly Gln 70 75 Arg Val Asp Thr Val Ile Gly Ala Val Pro Lys Ser Ile Leu Ile His 85 Thr Ile Asn Lys Tyr Leu 100

<210> 73 <211> 109 <212> PRT <213> Griffithsia pacifica

Met Ser Ile Ser Gln Val Ile Asp Thr Ser Phe His Glu Glu Val Ile 5 10 1 Asn Ser Arg Gln Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly 30 20 25 Pro Cys Arg Met Ile Ala Ser Thr Ile Asp Glu Ile Ala His Asp Tyr 35 Lys Asp Lys Leu Lys Val Val Lys Val Asn Thr Asp Gln Asn Pro Thr 55 Ile Ala Thr Glu Tyr Gly Ile Arg Ser Ile Pro Thr Val Met Ile Phe 70 75 Ile Asn Gly Lys Lys Val Asp Thr Val Val Gly Ala Val Pro Lys Leu 95 85 90 Thr Leu Leu Asn Thr Leu Gln Lys His Leu Lys Ser Thr

<210> 74 <211> 107 <212> PRT <213> Porphyra yezoensis

<400> 74 Met Ser Val Ser Gln Val Thr Asp Ala Ser Phe Lys Gln Glu Val Ile 1 . 5 10 Asn Asn Asn Leu Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly 20 25 Pro Cys Arg Met Val Ser Pro Val Val Asp Glu Ile Ala Glu Glu Tyr 35 40 Glu Ser Ser Ile Lys Val Val Lys Ile Asn Thr Asp Asp Asn Pro Thr 55 Ile Ala Ala Glu Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Ile Phe 70 75 Lys Ala Gly Glu Arg Val Asp Thr Val Ile Gly Ala Val Pro Lys Ser 85 90 Thr Leu Ala Ser Thr Leu Asn Lys Tyr Ile Ser

<210> 75 <211> 107 <212> PRT <213> Porphyra purpurea

<400> 75 Met Ser Val Ser Gln Val Thr Asp Ala Ser Phe Lys Gln Glu Val Ile

10 Asn Asn Asp Leu Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly 25 Pro Cys Arg Met Val Ser Pro Val Val Asp Ala Ile Ala Glu Glu Tyr 40 Glu Ser Ser Ile Lys Val Val Lys Ile Asn Thr Asp Asp Asn Pro Thr 55 Ile Ala Ala Glu Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Ile Phe 70 Lys Ser Gly Glu Arg Val Asp Thr Val Ile Gly Ala Val Pro Lys Ser 85 Thr Leu Glu Ser Thr Leu Asn Lys Tyr Ile Ser 100

<210> 76

<211> 114

<212> PRT

<213> Arabidopsis thaliana

<400> 76

Met Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro 40 Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val Leu Phe Leu Lys Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln 70 75 Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys 90 Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr Ile Ala Lys His 105 Leu Ala

<210> 77 <211> 110 <212> PRT

<213> Anabaena

<400> 77

Ser Lys Gly Val Ile Thr Ile Thr Asp Ala Glu Phe Glu Ser Glu Val Leu Lys Ala Glu Gln Pro Val Leu Val Tyr Phe Trp Ala Ser Trp Cys 25 Gly Pro Cys Gln Leu Met Ser Pro Leu Ile Asn Leu Ala Ala Asn Thr Tyr Ser Asp Arg Leu Lys Val Val Lys Leu Glu Ile Asp Pro Asn Pro 55 Thr Thr Val Lys Lys Tyr Lys Val Glu Gly Val Pro Ala Leu Arg Leu 70 75 Val Lys Gly Glu Gln Ile Leu Asp Ser Thr Glu Gly Val Ile Ser Lys 90 Asp Lys Leu Leu Ser Phe Leu Asp Thr His Leu Asn Asn Asn 100 105

<210> 78

<211> 123

<212> PRT

<213> Brassica napus

<400> 78

Met Ala Ala Thr Ala Glu Val Ile Pro Ala Gly Glu Val Ile Ala Cys 10 His Thr Val Glu Asp Trp Asn Asn Lys Leu Lys Ala Ala Lys Glu Ser 25 Asn Lys Leu Ile Val Ile Asp Phe Thr Ala Val Trp Cys Pro Fro Cys 40 Arg Phe Ile Ala Pro Ile Phe Val Glu Leu Ala Lys Lys His Leu Asp 55 Val Val Phe Phe Lys Val Asp Val Asp Glu Leu Ala Thr Val Ala Gln 70 Glu Phe Asp Val Gln Ala Met Pro Thr Phe Val Tyr Met Lys Gly Glu 90 85 Glu Lys Leu Asp Lys Val Val Gly Ala Ala Lys Glu Glu Ile Glu Ala 105 100 Lys Leu Leu Lys His Ser Gln Val Ala Ala Ala

<210> 79

<211> 126 <212> PRT

<213> Nicotiana tabacum

<210> 80 <211> 133 <212> PRT

<213> Arabidopsis thaliana

<400> 80 Met Gly Gly Ala Leu Ser Thr Val Phe Gly Ser Gly Glu Asp Ala Thr 10 Ala Ala Gly Thr Glu Ser Glu Pro Ser Arg Val Leu Lys Phe Ser Ser Ser Ala Arg Trp Gln Leu His Phe Asn Glu Ile Lys Glu Ser Asn Lys 40 Leu Leu Val Val Asp Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Met 55 60 Ile Glu Pro Ala Ile His Ala Met Ala Asp Lys Phe Asn Asp Val Asp 75 Phe Val Lys Leu Asp Val Asp Glu Leu Pro Asp Val Ala Lys Glu Phe Asn Val Thr Ala Met Pro Thr Phe Val Leu Val Lys Arg Gly Lys Glu 105 110 Ile Glu Arg Ile Ile Gly Ala Lys Lys Asp Glu Leu Glu Lys Lys Val 115 120 Ser Lys Leu Arg Ala 130

<210> 81 <211> 119 <212> PRT <213> Brassica napus

<400> 81 Met Ala Ala Glu Glu Gly Gln Val Ile Gly Cys His Glu Ile Asp Val Trp Ala Val Gln Leu Asp Thr Ala Lys Gln Ser Asn Lys Leu Ile Val 20 Ile Asp Phe Thr Ala Ser Trp Cys Pro Pro Cys Arg Met Ile Ala Pro 35 40 Val Phe Ala Asp Leu Ala Lys Lys Phe Met Ser Ser Ala Ile Phe Phe 55 Lys Val Asp Val Asp Glu Leu Gln Asn Val Ala Gln Glu Phe Gly Val 75 Glu Ala Met Pro Thr Phe Val Leu Ile Lys Asp Gly Asn Val Val Asp 85 90 Lys Val Val Gly Ala Arg Lys Glu Asp Leu His Ala Thr Ile Ala Lys 100 105 His Thr Gly Val Ala Thr Ala

<210> 82 <211> 118 . <212> PRT <213> Nicotiana tabacum

<400> 82

Met Ala Glu Glu Gly Gln Val Ile Gly Val His Thr Val Asp Ala Trp Asn Glu His Leu Gln Lys Gly Ile Asp Asp Lys Lys Leu Ile Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Lys Phe Ile Ala Ser Phe 40 Tyr Ala Glu Leu Ala Lys Lys Met Pro Thr Val Thr Phe Leu Lys Val 55 Asp Val Asp Glu Leu Lys Ser Val Ala Thr Asp Trp Ala Val Glu Ala 70 · 75 Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Val Asp Lys Val 90 Val Gly Ala Lys Lys Asp Glu Leu Gln Gln Thr Ile Ala Lys His Ile 100 105 Ser Ser Thr Ser Thr Ala 115

<210> 83 <211> 118 <212> PRT <213> Arabidopsis thaliana

100 105 110 Thr Val Val Ala Ala Ala 115

<210> 84 <211> 125 <212> PRT <213> Arabidopsis thaliana

Met Ala Ala Glu Glu Gly Gln Val Ile Gly Cys His Thr Asn Asp Val Trp Thr Val Gln Leu Asp Lys Ala Lys Glu Ser Asn Lys Leu Ile Val 25 Ile Asp Phe Thr Ala Ser Trp Cys Pro Pro Cys Arg Met Ile Ala Pro 40 Ile Phe Asn Asp Leu Ala Lys Lys Phe Met Ser Ser Ala Ile Phe Phe 55 Lys Val Asp Val Asp Glu Leu Gln Ser Val Ala Lys Glu Phe Gly Val 70 Glu Ala Met Pro Thr Phe Val Phe Ile Lys Ala Gly Glu Val Val Asp Lys Leu Val Gly Ala Asn Lys Glu Asp Leu Gln Ala Lys Ile Val Lys 100 105 His Thr Gly Val Thr Thr Val Val Asn Gln Phe Glu Ala

<210> 85 <211> 118 <212> PRT

115

<213> Arabidopsis thaliana

<400> 85 Met Ala Gly Glu Gly Glu Val Ile Ala Cys His Thr Leu Glu Val Trp 10 Asn Glu Lys Val Lys Asp Ala Asn Glu Ser Lys Lys Leu Ile Val Ile 20 25 Asp Phe Thr Ala Ser Trp Cys Pro Pro Cys Arg Phe Ile Ala Pro Val 40 Phe Ala Glu Met Ala Lys Lys Phe Thr Asn Val Val Phe Phe Lys Ile 55 Asp Val Asp Glu Leu Gln Ala Val Ala Gln Glu Phe Lys Val Glu Ala 70 75 Met Pro Thr Phe Val Phe Met Lys Glu Gly Asn Ile Ile Asp Arg Val 90 Val Gly Ala Ala Lys Asp Glu Ile Asn Glu Lys Leu Met Lys His Gly Gly Leu Val Ala Ser Ala 115

<210> 86 <211> 123 <212> PRT <213> Brassica rapa

<400> 86 Met Ala Ala Thr Ala Glu Leu Ile Pro Ala Gly Glu Val Ile Ala Cys His Thr Val Glu Asp Trp Asn Asn Lys Leu Lys Ala Ala Lys Glu Ser 25 30 Asn Lys Leu Ile Val Ile Asp Phe Thr Ala Val Trp Cys Pro Pro Cys 45 Arg Phe Ile Ala Pro Ile Phe Val Glu Leu Ala Lys Lys His Leu Asp

 Val
 Val
 Phe
 Lys
 Val
 Asp
 Val
 Asp
 Glu
 Leu
 Ala
 Thr
 Val
 Ala
 Lys
 80
 Glu
 Phe
 Val
 Tyr
 Met
 Lys
 Gly
 Glu
 Ala
 Ala
 Ala
 Lys
 Glu
 Glu
 Ala
 Al

<210> 87

<211> 112

<212> PRT

<213> Chlamydomonas reinhardtii

<400> 87

<210> 88

<211> 116

<212> PRT

<213> Fagopyrum esculentum

<400> 88

Met Ala Glu Glu Ala Gln Val Ile Ala Cys His Thr Val Gln Glu Trp Asn Glu Lys Phe Gln Lys Ala Lys Asp Ser Gly Lys Leu Ile Val Ile Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Thr Pro Tyr 35 40 Val Ser Glu Leu Ala Lys Lys Phe Pro His Val Ala Phe Phe Lys Val . 55 Asp Val Asp Asp Leu Lys Asp Val Ala Glu Glu Tyr Lys Val Glu Ala 70 Met Pro Ser Phe Val Ile Leu Lys Glu Gly Gln Glu Val Glu Arg Ile 85 90 Val Gly Ala Arg Lys Asp Glu Leu Leu His Lys Ile Ala Val His Ala 100 105 Pro Ile Thr Ala 115

<210> 89

<211> 122

<212> PRT

<213> Oryza sativa

<400> 89

Met Ala Ala Glu Glu Gly Val Val Ile Ala Cys His Asn Lys Asp Glu

1 5 10 15

Phe Asp Ala Gln Met Thr Lys Ala Lys Glu Ala Gly Lys Val Val Ile
20 25 30

Ile Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro

Val Phe Ala Glu Tyr Ala Lys Lys Phe Pro Gly Ala Val Phe Leu Lys 50

Val Asp Val Asp Glu Leu Lys Glu Val Ala Glu Lys Tyr Asn Val Glu 65

Ala Met Pro Thr Phe Leu Phe Ile Lys Asp Gly Ala Glu Ala Asp Lys 85

Val Val Gly Ala Arg Lys Asp Asp Leu Gln Asn Thr Ile Val Lys His 100

Val Gly Ala Thr Ala Ala Ser Ala Ser Ala 120

<210> 90 <211> 125 <212> PRT <213> Picea mariana

<400> 90 Met Ala Glu Gly Asn Val Phe Ala Cys His Ser Thr Glu Gly Trp Arg 10 Ser Lys Leu Gln Glu Ala Ile Asp Thr Lys Arg Leu Val Ala Val Asp 20 25 Phe Thr Ala Thr Trp Cys Gly Pro Cys Arg Val Ile Gly Pro Val Phe 40 45 Val Glu Leu Ser Lys Lys Phe Pro Glu Ile Phe Phe Leu Lys Val Asp 55 Val Asp Glu Leu Arg Asp Val Ala Gln Glu Trp Asp Val Glu Ala Met 70 Pro Thr Phe Ile Phe Ile Lys Asp Gly Lys Ala Val Asp Lys Val Val 85 90 Gly Ala Lys Lys Asp Asp Leu Glu Arg Lys Val Ala Ala Leu Ala Ala 105 100 Ala Ala Thr Thr Thr Glu Ala Thr Leu Pro Ala Gln Ala

120

<210> 91 <211> 118 <212> PRT <213> Ricinus communis

<213> RICINUS COMMUNIS

<400> 91 Met Ala Ala Glu Glu Gly Gln Val Ile Gly Cys His Thr Val Glu Ala 10 Trp Asn Glu Gln Leu Gln Lys Gly Asn Asp Thr Lys Gly Leu Ile Val 25 Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro Phe Leu Ala Glu Leu Ala Lys Lys Leu Pro Asn Val Thr Phe Leu Lys 55 Val Asp Val Asp Glu Leu Lys Thr Val Ala His Glu Trp Ala Val Glu 70 75 Ser Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Met Asp Lys 90 95 Val Val Gly Ala Lys Lys Asp Glu Leu Gln Gln Thr Ile Ala Lys His 100 105 Met Ala Thr Ala Ser Thr 115

<210> 92 <211> 126 <212> PRT <213> triticum aestivum <400> 92

<210> 93 <211> 109 <212> PRT <213> Aspergillus nidulans

<210> 94 <211> 105 <212> PRT <213> Alicyclobacillus

<210> 95 <211> 91 <212> PRT <213> Archaeoglobus fulgidus

<210> 96 <211> 103 <212> PRT <213> Bacillus subtilis

<210> 97 <211> 87 <212> PRT <213> Bacteriophage T4

100

<210> 98 <211> 117 <212> PRT <213> Borrelia burgdorferi

85

```
Ile Asp Phe Tyr Ala Asn Trp Cys Gly Pro Cys Lys Met Leu Ser Pro
Ile Phe Glu Lys Leu Ser Lys Lys Tyr Glu Asn Ser Ile Asp Phe Tyr
                        55
                                            60
Lys Val Asp Thr Asp Lys Glu Gln Asp Ile Ser Ser Ala Ile Gly Val
                    70
Gln Ser Leu Pro Thr Ile Leu Phe Ile Pro Val Asp Gly Lys Pro Lys
                                    90
                85
Val Ser Val Gly Phe Leu Gln Glu Asp Ala Phe Glu Asn Ile Ile Lys
            100
                                105
Asp Phe Phe Gly Phe
        115
<210> 99
<211> 108
<212> PRT
<213> Buchnera aphidicola
<400> 99
Met Asn Lys Ile Ile Glu Leu Thr Asp Gln Asn Phe Glu Glu Gln Val
                                    10
Leu Asn Ser Lys Ser Phe Phe Leu Val Asp Phe Trp Ala Gln Trp Cys
            20
Asn Pro Cys Lys Ile Leu Ala Pro Ile Leu Glu Glu Ile Ser Lys Glu
                            40
Tyr Ser Asn Lys Val Ile Val Gly Lys Leu Asn Ile Glu Glu Asn Pro
                        55
                                            60
Asn Thr Ala Pro Val Tyr Ser Ile Arg Ser Ile Pro Thr Leu Leu Leu
                    70
                                        75
Phe Asn Asn Ser Glu Val Leu Ala Thr Lys Val Gly Ala Val Ser Lys
                85
                                    90
Leu Glu Leu Lys Glu Phe Leu Asp Glu Asn Ile Asn
<210> 100
<211> 108
<212> PRT
<213> aphidicola
<400> 100
Met Asn Lys Ile Ile Glu Leu Thr Asp Gln Asn Phe Glu Lys Glu Val
                                    10
Leu Glu His Lys Ser Phe Val Leu Val Asp Phe Trp Ala Glu Trp Cys
            20
Asn Pro Cys Lys Ile Leu Ala Pro Ile Leu Glu Glu Ile Ala Gln Glu
                            40
Tyr Phe Asn Lys Ile Lys Val Gly Lys Leu Asn Ile Glu Lys Asn Pro
                        55
                                            60
Asn Thr Ala Pro Ile Tyr Ser Ile Arg Gly Ile Pro Ala Leu Leu Leu
                                        75
                    70
Phe His Gly Arg Glu Val Leu Ala Thr Lys Val Gly Ala Ile Ser Lys
                85
                                    90
Leu Gln Leu Lys Asp Phe Leu Asp Glu Asn Ile Lys
            100
<210> 101
<211> 108
<212> PRT
<213> Chlorobium limicola
<220>
<221> VARIANT
<222> 16, 17, 38, 42, 45, 54, 55, 58, 66, 72, 75, 79, 80, 81, 94,
99, 103
```

<223> Xaa = Any Amino Acid

<400> 101 Ala Gly Lys Tyr Phe Glu Ala Thr Asp Lys Asn Phe Gln Thr Glu Xaa 10 Xaa Asp Ser Asp Lys Ala Val Leu Val Asp Phe Trp Ala Ser Trp Cys 20 25 Gly Pro Cys Met Met Xaa Gly Pro Val Xaa Glu Gln Xaa Ala Asp Asp 40 Tyr Glu Gly Lys Ala Xaa Xaa Ala Lys Xaa Asn Val Asp Glu Asn Pro 60 55 Asn Xaa Ala Gly Gln Tyr Gly Xaa Arg Ser Xaa Pro Thr Met Xaa Xaa 70 Xaa Lys Gly Gly Lys Val Val Asp Gln Met Val Gly Ala Xaa Pro Lys Asn Met Xaa Ala Lys Lys Xaa Asp Glu His Ile Gly 105

<210> 102 <211> 102 <212> PRT

<213> Chlamydia muridarum

<210> 103 <211> 102 <212> PRT <213> Chlamydia pneumoniae

<210> 104 <211> 102 <212> PRT <213> Psittaci PCT/US01/50240

```
WO 02/50289
<400> 104
Met Val Lys Val Val Ser Ala Glu Asn Phe Asn Ser Phe Ile Ala Thr
                                    10
Gly Leu Val Leu Ile Asp Phe Phe Ala Glu Trp Cys Gly Pro Cys Lys
Met Leu Thr Pro Val Leu Glu Ser Leu Glu Ala Glu Val Ser Ser Val
        35
                            40
                                                45
Leu Ile Gly Lys Val Asn Ile Asp Asp His Pro Ala Pro Ala Glu Gln
Tyr Gly Val Ser Ser Ile Pro Thr Leu Ile Leu Phe Lys Asp Gly Lys
                    70
                                        75
Glu Val Asp Arg Val Val Gly Leu Lys Asp Lys Asp Ser Leu Ile Arg
                85
                                    90
Leu Ile Asn Gln His Ser
            100
<210> 105
<211> 102
<212> PRT
<213> Chlamydia trachomatis
<400> 105
Met Val Gln Val Val Ser Gln Glu Asn Phe Ala Asp Ser Ile Ala Ser
                                    10
Gly Leu Val Leu Ile Asp Phe Phe Ala Glu Trp Cys Gly Pro Cys Lys
                                25
Met Leu Thr Pro Val Leu Glu Ala Leu Ala Ala Glu Leu Pro His Val
Thr Ile Leu Lys Val Asp Ile Asp Ser Ser Pro Arg Pro Ala Glu Gln
 50
                        55
                                            60
Tyr Ser Val Ser Ser Ile Pro Thr Leu Ile Leu Phe Lys Asp Gly Lys
```

70 75 Glu Val Glu Arg Ser Val Gly Leu Lys Asp Lys Asp Ser Leu Ile Lys 85 90

Leu Ile Ser Lys His Gln 100

<210> 106 · <211> 105 <212> PRT

<213> Cornybacterium nephridii

<400> 106 Ala Thr Val Lys Val Asp Asn Ser Asn Phe Gln Ser Asp Val Leu Gln 10 Ser Ser Glu Pro Val Val Val Asp Phe Trp Ala Glu Trp Cys Gly Pro 30 Cys Lys Met Ile Ala Pro Ala Leu Asp Glu Ile Ala Thr Glu Met Ala 40 Gly Gln Val Lys Ile Ala Lys Val Asn Ile Asp Glu Asn Pro Glu Leu 55 60 Ala Ala Gln Phe Gly Val Arg Ser Ile Pro Thr Leu Leu Met Phe Lys 75 Asp Gly Glu Leu Ala Ala Asn Met Val Gly Ala Ala Pro Lys. Ser Arg Leu Ala Asp Trp Ile Lys Ala Ser Ala 100

<210> 107 <211> 107 <212> PRT <213> Cornybacterium nephridii <400> 107

 Ser Ala Thr Ile 1
 Val Asn Thr Thr Asp Glu Asn Phe Gln Ala Asp Val 1

 Leu Asp Ala Glu Thr 20
 Val Leu Val Asp Phe Trp Ala Gly Trp Cys 30

 Ala Pro Cys Lys Ala Ile Ala Pro Val Leu Glu Glu Leu Ser Asn Glu 35

 Tyr Ala Gly Lys Val Lys Ile Val Lys Val Asp Val Thr Ser Cys Glu 50

 Asp Thr Ala Val Lys Tyr Asn Ile Arg Asn Ile 65

 Phe Lys Asp Gly Glu Val Val Val Ala Gln Gln Val Gly Ala Ala Pro Arg 90

 Ser Lys Leu Ala Ala Phe Ile Asp Gln Asn Ile 100

<210> 108 <211> 145 <212> PRT

<213> Cornybacterium nephridii

<400> 108 Met Ile Ile Val Cys Ala Ser Cys Gly Ala Lys Asn Arg Val Pro Glu Glu Lys Leu Ala Val His Pro Asn Cys Gly Gln Cys His Gln Ala Leu 25 30 Leu Pro Leu Glu Pro Ile Glu Leu Asn Glu Gln Asn Phe Ser Asn Phe 35 40 Ile Ser Asn Ser Asp Leu Pro Val Leu Ile Asp Leu Trp Ala Glu Trp 55 Cys Gly Pro Cys Lys Met Met Ala Pro His Phe Ala Gln Val Ala Lys 75 70 Gln Asn Pro Tyr Val Val Phe Ala Lys Ile Asp Thr Glu Ala Asn Pro 85 90 Arg Leu Ser Ala Ala Phe Asn Val Arg Ser Ile Pro Thr Leu Val Leu 105 Met Asn Lys Thr Thr Glu Val Ala Arg Ile Ser Gly Ala Leu Arg Thr 120 Leu Glu Leu Gln Gln Trp Leu Asp Gln Gln Leu Gln Gln Gln Gly Asn

<210> 109 <211> 107 <212> PRT <213> Chromatium vinosum <220> <221> VARIANT <222> 17, 38, 42, 55, 58, 60, 72, 107

145

<223> Xaa = Any Amino Acid <400> 109

 Ser
 Asp
 Ser
 Ile
 Val
 His
 Val
 Thr
 Asp
 Asp
 Ser
 Phe
 Glu
 Glu
 Glu
 Val

 1
 1
 1
 1
 1
 1
 1
 15
 1
 15
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1

Ser Gln Leu Thr Ala Phe Leu Asp Ser Asn Xaa

<210> 110

<211> 107

<212> PRT

<213> Clostridium litorale

<400> 110

 Met
 Leu
 Asp
 Lys
 Asp
 Thr
 Phe
 Lys
 Thr
 Glu
 Val
 Leu
 Glu
 Fro
 Cys
 Val
 Leu
 Cys
 Asp
 Glu
 Glu
 Glu
 Leu
 Ser
 Lys
 Lys
 Lys
 Tyr
 Glu
 Glu
 Glu
 Leu
 Ser
 Lys
 Lys
 Lys
 Glu
 Glu
 Glu
 Leu
 Ser
 Lys
 Lys
 Lys
 Glu
 Glu
 Glu
 Leu
 Ser
 Lys
 Lys
 Lys
 Lys
 Lys
 Lys
 Lys
 Asp
 Lys
 Asp
 Asp
 Asp
 Asp
 Ala
 Thr
 Inch
 Inch</

85 90 Ile Glu Ala Met Val Glu Glu His Ile Ser Lys

<210> 111

<211> 40

<212> PRT

<213> Clostridium sporogenes

<400> 111

<210> 112

<211> 33

<212> PRT

<213> Clostridium sticklandii

<400> 112

Met Phe Glu Leu Asp Lys Asp Thr Phe Glu Thr Glu Val Leu Gln Gly
1 5 10 15

Thr Gly Tyr Val Leu Val Asp Phe Trp Ser Glu Gly Cys Glu Pro Cys
20 25 30

Lys

<210> 113

<211> 106

<212> PRT

<213> Coprinus comatus

<400> 113

50 | 55 | 60 | 60 | 11e | Ser | Glu | Glu | Ala | Lys | Ile | Arg | Ala | Met | Pro | Thr | Phe | Gln | Val | Tyr | 65 | 70 | 75 | 80 | 80 | Lys | Asp | Gly | Gln | Lys | Ile | Asp | Glu | Leu | Val | Gly | Ala | Asn | Pro | Thr | Ala | 85 | 90 | 95 | Ser | Leu | Ala | 100 | 105 | Ser | Leu | Ala | 105 | Ser | Leu |

<210> 114

<211> 105

<212> PRT

<213> Dictyostelium discoideum

<400> 114

Met Ser Asn Arg Val Ile His Val Ser Ser Cys Glu Glu Leu Asp Lys 1 10 His Leu Arg Asp Glu Arg Val Val Val Asp Phe Ser Ala Val Trp Cys 20 25 Gly Pro Cys Arg Ala Ile Ser Pro Val Phe Glu Lys Leu Ser Asn Glu Phe Ile Thr Phe Thr Phe Leu His Val Asp Ile Asp Lys Leu Asn Val 55 60 His Pro Ile Val Ser Lys Ile Lys Ser Val Pro Thr Phe His Phe Tyr 70 Arg Asn Gly Ser Lys Val Ser Glu Phe Ser Gly Ala Ser Glu Ser Ile 85 90 Leu Arg Ser Thr Leu Glu Ala Asn Lys

<210> 115

<211> 88

<212> PRT

<213> Dictyostelium discoideum

<400> 115

 Met
 Ser
 Arg
 Val
 Ile
 His
 Ile
 Ser
 Ser
 Asn
 Glu
 Glu
 Leu
 His
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15
 15<

<210> 116

<211> 88

<212> PRT

<213> Dictyostelium discoideum

<400> 116

 Met
 Ser
 Arg
 Val
 Ile
 His
 Ile
 Ser
 Asn
 Glu
 Glu
 Leu
 Als
 Lys
 His

 Leu
 Gln
 Ala
 Glu
 Arg
 Leu
 Val
 Ile
 Asp
 Phe
 Ser
 Ala
 Ala
 Trp
 Cys
 Gly

 Pro
 Cys
 Arg
 Ala
 Ile
 Ser
 Pro
 Val
 Phe
 Glu
 Lys
 Leu
 Ser
 Glu
 Phe

 Val
 Thr
 Phe
 Val
 His
 Val
 Asp
 Ile
 Asp
 Lys
 Leu
 Ser
 Gly
 His

 50
 55
 55
 60
 60
 Fro
 Phe
 Tyr
 Phe
 Tyr
 Arg

 65
 70
 70
 75
 Thr
 Phe
 Tyr
 Phe

PCT/US01/50240 WO 02/50289

Asn Gly Ala Lys Val Ser Glu Phe

<210> 117 <211> 108 <212> PRT <213> E coli, salmonella typhimurium

<400> 117 Ser Asp Lys Ile Ile His Leu Thr Asp Asp Ser Phe Asp Thr Asp Val Leu Lys Ala Asp Gly Ala Ile Leu Val Asp Phe Trp Ala Glu Trp Cys Gly Pro Cys Lys Met Ile Ala Pro Ile Leu Asp Glu Ile Ala Asp Glu Tyr Gln Gly Lys Leu Thr Val Ala Lys Leu Asn Ile Asp Gln Asn Pro 55 Gly Thr Ala Pro Lys Tyr Gly Ile Arg Gly Ile Pro Thr Leu Leu Leu 70 75 Phe Lys Asn Gly Glu Val Ala Ala Thr Lys Val Gly Ala Leu Ser Lys 85 90 Gly Gln Leu Lys Glu Phe Leu Asp Ala Asn Leu Ala

<210> 118 <211> 105 <212> PRT <213> Synechocystis

<400> 118 Met Ala Val Lys Lys Gln Phe Ala Asn Phe Ala Glu Met Leu Ala Gly 10 Ser Pro Lys Pro Val Leu Val Asp Phe Tyr Ala Thr Trp Cys Gly Pro 30 20 25 Cys Gln Met Met Ala Pro Ile Leu Glu Gln Val Gly Ser His Leu Arg Gln Gln Ile Gln Val Val Lys Ile Asp Thr Asp Lys Tyr Pro Ala Ile 55 Ala Thr Gln Tyr Gln Ile Gln Ser Leu Pro Thr Leu Val Leu Phe Lys 75 70 Gln Gly Gln Pro Val His Arg Met Glu Gly Val Gln Gln Ala Ala Gln 85 90 Leu Ile Gln Gln Leu Gln Val Phe Val

<210> 119 <211> 139 <212> PRT <213> E. coli

<400> 119 Met Asn Thr Val Cys Thr His Cys Gln Ala Ile Asn Arg Ile Pro Asp Asp Arg Ile Glu Asp Ala Ala Lys Cys Gly Arg Cys Gly His Asp Leu 25 Phe Asp Gly Glu Val Ile Asn Ala Thr Gly Glu Thr Leu Asp Lys Leu Leu Lys Asp Asp Leu Pro Val Val Ile Asp Phe Trp Ala Pro Trp Cys 50 55 Gly Pro Cys Arg Asn Phe Ala Pro Ile Phe Glu Asp Val Ala Gln Glu 70 75 Arg Ser Gly Lys Val Arg Phe Val Lys Val Asn Thr Glu Ala Glu Arg 85 90 Glu Leu Ser Ser Arg Phe Gly Ile Arg Ser Ile Pro Thr Ile Met Ile

```
105
            100
Phe Lys Asn Gly Gln Val Val Asp Met Leu Asn Gly Ala Val Pro Lys
                            120
Ala Pro Phe Asp Ser Trp Leu Asn Glu Ser Leu
    130
                        135
<210> 120
<211> 110
<212> PRT
<213> Eubacterium acidaminophilum
<400> 120
Met Ser Ala Leu Leu Val Glu Ile Asp Lys Asp Gln Phe Gln Ala Glu
                                    10
Val Leu Glu Ala Glu Gly Tyr Val Leu Val Asp Tyr Phe Ser Asp Gly
Cys Val Pro Cys Lys Ala Leu Met Pro Asp Val Glu Glu Leu Ala Ala
Lys Tyr Glu Gly Lys Val Ala Phe Arg Lys Phe Asn Thr Ser Ser Ala
                                            60
                        55
Arg Arg Leu Ala Ile Ser Gln Lys Ile Leu Gly Leu Pro Thr Ile Thr
Leu Tyr Lys Gly Gly Gln Lys Val Glu Glu Val Thr Lys Asp Asp Ala
Thr Arg Glu Asn Ile Asp Ala Met Ile Ala Lys His Val Gly
<210> 121
<211> 107
<212> PRT
<213> Haemophilus influenzae
<400> 121
Met Ser Glu Val Leu His Ile Asn Asp Ala Asp Phe Glu Ser Val Val
                                    10
Val Asn Ser Asp Ile Pro Ile Leu Leu Asp Phe Trp Ala Pro Trp Cys
Gly Pro Cys Lys Met Ile Ala Pro Val Leu Asp Glu Leu Ala Pro Glu
Phe Ala Gly Lys Val Lys Ile Val Lys Met Asn Val Asp Asp Asn Gln
                        55
Ala Thr Pro Ala Gln Phe Gly Val Arg Ser Ile Pro Thr Leu Leu Leu
Ile Lys Asn Gly Gln Val Val Ala Thr Gln Val Gly Ala Leu Pro Lys
                85
                                    90
Thr Gln Leu Ala Asn Phe Ile Asn Gln His Ile
<210> 122
<211> 167
<212> PRT
<213> Haemophilus influenzae
<400> 122
Met Lys Ile Lys Lys Leu Leu Lys Asn Gly Leu Ser Leu Phe Leu Thr
                                    10
Phe Ile Val Ile Thr Ser Ile Leu Asp Phe Val Arg Arg Pro Val Val
                                25
Pro Glu Glu Ile Asn Lys Ile Thr Leu Gln Asp Leu Gln Gly Asn Thr
        35
                            40
Phe Ser Leu Glu Ser Leu Asp Gln Asn Lys Pro Thr Leu Leu Tyr Phe
                        55
                                            60
Trp Gly Thr Trp Cys Gly Tyr Cys Arg Tyr Thr Ser Pro Ala Ile Asn
                    70
```

Ser Leu Ala Lys Glu Gly Tyr Gln Val Val Ser Val Ala Leu Arg Ser Gly Asn Glù Ala Asp Val Asn Asp Tyr Leu Ser Lys Asn Asp Tyr His 105 100 110 Phe Thr Thr Val Asn Asp Pro Lys Gly Glu Phe Ala Glu Arg Trp Gln 115 120 125 Ile Asn Val Thr Pro Thr Ile Val Leu Leu Ser Lys Gly Lys Met Asp 135 140 Leu Val Thr Thr Gly Leu Thr Ser Tyr Trp Gly Leu Lys Val Arg Leu 150 155 Phe Phe Ala Glu Phe Phe Gly

<210> 123

<211> 106

<212> PRT

<213> Helicobacter pylori

<400> 123

 Met
 Ser
 His
 Tyr
 Ile
 Glu
 Leu
 Thr
 Glu
 Glu
 Asn
 Phe
 Glu
 Ser
 Thr
 Ile
 Ile</th

<210> 124

<211> 103

<212> PRT

<213> Listeria monocytogenes

<400> 124

Met Val Lys Glu Ile Thr Asp Ala Thr Phe Glu Gln Glu Thr Ser Glu 1.0 Gly Leu Val Leu Thr Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Arg 25 Met Val Ala Pro Val Leu Glu Glu Ile Gln Glu Glu Arg Gly Glu Ala 40 Leu Lys Ile Val Lys Met Asp Val Asp Glu Asn Pro Glu Thr Pro Gly 55 Ser Phe Gly Val Met Ser Ile Pro Thr Leu Leu Ile Lys Lys Asp Gly 70 75 Glu Val Val Glu Thr Ile Ile Gly Tyr Arg Pro Lys Glu Glu Leu Asp 85 90 Glu Val Ile Asn Lys Tyr Val 100

<210> 125

<211> 85

<212> PRT

<213> Methoanococus jannaschii

<400> 125

Met Ser Lys Val Lys Ile Glu Leu Phe Thr Ser Pro Met Cys Pro His 1 15 Cys Pro Ala Ala Lys Arg Val Val Glu Glu Val Ala Asn Glu Met Pro

20 25 30

Asp Ala Val Glu Val Glu Tyr Ile Asn Val Met Glu Asn Pro Gln Lys
35 40 45

Ala Met Glu Tyr Gly Ile Met Ala Val Pro Thr Ile Val Ile Asn Gly
50 55 60

Asp Val Glu Phe Ile Gly Ala Pro Thr Lys Glu Ala Leu Val Glu Ala
65 70 75 80

Ile Lys Lys Arg Leu
85

<210> 126

<211> 102 <212> PRT

<213> Mycoplasma genitalium

<210> 127

<211> 458

<212> PRT

<213> mycobacterium leprae

100

<400> 127 Met Asn Thr Thr Pro Ser Ala His Glu Thr Ile His Glu Val Ile Val 10 Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Ala Ala Arg 25 Ala Gln Leu Thr Pro Leu Val Phe Glu Gly Thr Ser Phe Gly Gly Ala 35 40 Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg 70 Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg 90 Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala 105 Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile 125 115 120 Pro Gly Glu Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr 135 140 Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly 150 155 Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg 165 170 Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile 180 185 190 Met Leu Gly Arg Ala Arg Asn Asn Asp Lys Ile Lys Phe Ile Thr Asn 200 205 His Thr Val Val Ala Val Asn Gly Tyr Thr Thr Val Thr Gly Leu Arg

PCT/US01/50240 WO 02/50289

```
Leu Arg Asn Thr Thr Thr Gly Glu Glu Thr Thr Leu Val Val Thr Gly
                    230
                                        235
Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Ser Leu Val Ser Asp
                                   250
                245
Val Val Asp Ile Asp Pro Asp Gly Tyr Val Leu Val Lys Gly Arg Thr
                                265
            260
                                                    270
Thr Ser Thr Ser Met Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp
                            280
Arg Thr Tyr Arg Gln Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala
                       295
                                            300
Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Gly Ser Lys Ala
                    310
                                       315
Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr Thr
                                    330
                325
Asp Trp Ser Thr Ala Met Thr Asp Ala Lys Asn Ala Gly Val Thr Ile
                               345
                                                    350
           340
Glu Val Thr Asp Ala Ser Phe Phe Ala Asp Val Leu Ser Ser Asn Lys
                           360
                                               365
Pro Val Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Lys Met
                        3.75
                                            380
Val Ala Pro Val Leu Glu Glu Ile Ala Ser Glu Gln Arg Asn Gln Leu
                    390
                                       395
Thr Val Ala Lys Leu Asp Val Asp Thr Asn Pro Glu Met Ala Arg Glu
                405
                                   410
                                                       415
Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gly Gln
                                425
            420
                                                    430
Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg
                           440
       435
                                               445
Asp Leu Ser Asp Val Val Pro Asn Leu Asn
                        455
```

<210> 128

<211> 102

<212> PRT

<213> Mycoplasma pneumoniae

<400> 128

Met Val Thr Glu Ile Lys Ser Leu Lys Gln Leu Gly Glu Leu Phe Ala 10 Ser Asn Asn Lys Val Ile Ile Asp Phe Trp Ala Glu Trp Cys Gly Pro 20 25 Cys Lys Ile Thr Gly Pro Glu Phe Ala Lys Ala Ala Ser Glu Val Ser 40 Thr Val Ala Phe Ala Lys Val Asn Val Asp Glu Gln Thr Asp Ile Ala 55 60 Ala Ala Tyr Lys Ile Thr Ser Leu Pro Thr Ile Val Leu Phe Glu Lys 70 75 Gly Gln Glu Lys His Arg Ala Ile Gly Phe Met Pro Lys Ala Lys Ile 85 Val Gln Leu Val Ser Gln

100

<210> 129

<211> 112

<212> PRT <213> Mycobacterium smegmatis

<400> 129

Met Ser Glu Asp Ser Ala Thr Val Ala Val Thr Asp Asp Ser Phe Ser Thr Asp Val Leu Gly Ser Ser Lys Pro Val Leu Val Asp Phe Trp Ala 25 Thr Trp Cys Gly Pro Cys Lys Met Val Ala Pro Val Leu Glu Glu Ile 40 Ala Ala Glu Lys Gly Asp Gln Leu Thr Val Ala Lys Ile Asp Val Asp

```
55
Val Asp Ala Asn Pro Ala Thr Ala Arg Asp Phe Gln Val Val Ser Ile
                                         75
                    70
Pro Thr Met Ile Leu Phe Lys Asp Gly Ala Pro Val Lys Arg Ile Val
                85
                                    90
Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg Glu Leu Ser Asp Ala Leu
                                 105
                                                     110
<210> 130
<211> 115
<212> PRT
<213> Mycobacterium tuberculosis
<400> 130
Thr Asp Ser Glu Lys Ser Ala Thr Ile Lys Val Thr Asp Ala Ser Phe
                                    10
Ala Thr Asp Val Leu Ser Ser Asn Lys Pro Val Leu Val Asp Phe Trp
            20
                                25
Ala Thr Trp Cys Gly Pro Cys Lys Met Val Ala Pro Val Leu Glu Glu
                            40
Ile Ala Thr Glu Arg Ala Thr Asp Leu Thr Val Ala Lys Leu Asp Val
                        55
                                             60
Asp Thr Asn Pro Glu Thr Ala Arg Asn Phe Gln Val Val Ser Ile Pro
Thr Leu Ile Leu Phe Lys Asp Gly Gln Pro Val Lys Arg Ile Val Gly
                                    90
Ala Lys Gly Lys Ala Ala Leu Leu Arg Glu Leu Ser Asp Val Val Pro
            100
                                105
Asn Leu Asn
        115
<210> 131
<211> 127
<212> PRT
<213> Neurospora crassa
<400> 131
Met Ser Asp Gly Val Lys His Ile Asn Ser Ala Gln Glu Phe Ala Asn
Leu Leu Asn Thr Thr Gln Tyr Val Val Ala Asp Phe Tyr Ala Asp Trp
           20
Cys Gly Pro Cys Lys Ala Ile Ala Pro Met Tyr Ala Gln Phe Ala Lys
                            40
Thr Phe Ser Ile Pro Asn Phe Leu Ala Phe Ala Lys Ile Asn Val Asp
Ser Val Gln Gln Val Ala Gln His Tyr Arg Val Ser Ala Met Pro Thr
                                        75
Phe Leu Phe Phe Lys Asn Gly Lys Gln Val Ala Val Asn Gly Ser Val
                85
                                    90
Met Ile Gln Gly Ala Asp Val Asn Ser Leu Arg Ala Ala Ala Glu Lys
            100
                                105
Met Gly Arg Leu Ala Lys Glu Lys Ala Ala Ala Ala Gly Ser Ser
<210> 132
<211> 106
<212> PRT
<213> Penicillium chrysogenum
<400> 132
Met Gly Val Thr Pro Ile Lys Ser Val Ala Glu Tyr Lys Glu Lys Val
Thr Asp Ala Thr Gly Pro Val Val Val Asp Phe His Ala Thr Trp Cys
            20
```

1.1

Gly Pro Cys Lys Ala Ile Ala Pro Ala Leu Glu Lys Leu Ser Glu Thr
35

His Thr Gly Ile Gln Phe Tyr Lys Val Asp Val Asp Glu Leu Ser Glu
50

Val Ala Ala Ser Asn Gly Val Ser Ala Met Pro Thr Phe His Phe Tyr
65

To 70

Lys Gly Gly Glu Arg Asn Glu Glu Val Lys Gly Ala Asn Pro Ala Ala
85

90

11e Gln Ala Gly Val Lys Ala Ile Leu Glu
105

<210> 133

<211> 108

<212> PRT

<213> Pseudomonas aeruginosa

<400> 133

 Met
 Ser
 Glu
 His
 Ile
 Val
 Asn
 Val
 Thr
 Asp
 Ala
 Ser
 Phe
 Glu
 Gln
 Asp

 Val
 Leu
 Leu
 Val
 Asp
 Tyr
 Trp
 Ala
 Glu
 Trp

 Cys
 Gly
 Pro
 Cys
 Lys
 Met
 Ile
 Ala
 Pro
 Val
 Leu
 Asp
 Glu
 Val
 Ala
 Arg
 Glu
 Val
 Ala
 Arg
 Glu
 Asp
 Ile
 <210> 134

<211> 104

<212> PRT

<213> Rhodospirillum rubrum

<220>

<221> VARIANT

<222> 21, 35

<223> Xaa = Any Amino Acid

<400> 134

 Met
 Lys
 Gln
 Val
 Ser
 Asp
 Ala
 Ser
 Phe
 Glu
 Glu
 Asp
 Val
 Leu
 Lys
 Ala

 Asp
 Gly
 Pro
 Asn
 Xaa
 Val
 Asp
 Phe
 Trp
 Ala
 Glu
 Trp
 Cys
 Gly
 Pro
 Cys
 30
 Cys
 Asp
 45
 Cys
 Asp
 45
 Cys
 Asp
 45
 Cys
 Asp
 60
 Asp
 Fro
 Glu
 Asp
 Fro
 Thr
 Leu
 Met
 Ile
 Phe
 Lys
 Asp
 Asp
 Asp
 Fro
 Thr
 Leu
 Pro
 Lys
 Thr
 Lys
 Thr
 Lys
 Thr
 Lys
 Thr
 Lys
 Thr<

Phe Glu Trp Val Glu Ala Ser Val

<210> 135

<211> 105

<212> PRT

<213> Rhodobacter sphaeroides

<400> 135

```
Ser Thr Val Pro Val Thr Asp Ala Thr Phe Asp Thr Glu Val Arg Lys
                                    10
Ser Asp Val Pro Val Val Val Asp Phe Trp Ala Glu Trp Cys Gly Pro
                                25
Cys Arg Gln Ile Gly Pro Ala Leu Glu Glu Leu Ser Lys Glu Tyr Ala
                            40
Gly Lys Val Lys Ile Val Lys Val Asn Val Asp Glu Asn Pro Glu Ser
                        55
Pro Ala Met Leu Gly Val Arg Gly Ile Pro Ala Leu Phe Leu Phe Lys
                    70
                                        75
Asn Gly Gln Val Val Ser Asn Lys Val Gly Ala Ala Pro Lys Ala Ala
Leu Ala Thr Trp Ile Ala Ser Ala Leu
           100
```

<210> 136 <211> 130

<212> PRT

<213> Rickettsia prowazekii

<400> 136

Met Ser Cys Tyr Asn Glu Ile Thr Thr Leu Leu Glu Phe Asp Ser Asn Asp Ile Asn Thr Thr Gln Arg Ile Asn Met Val Asn Asn Val Thr Asp 20 25 Ser Ser Phe Lys Asn Glu Val Leu Glu Ser Asp Leu Pro Val Met Val 40 45 Asp Phe Trp Ala Glu Trp Cys Gly Pro Cys Lys Met Leu Ile Pro Ile 55 Ile Asp Glu Ile Ser Lys Glu Leu Gln Asp Lys Val Lys Val Leu Lys Met Asn Ile Asp Glu Asn Pro Lys Thr Pro Ser Glu Tyr Gly Ile Arg 90 85 Ser Ile Pro Thr Ile Met Leu Phe Lys Asn Gly Glu Gln Lys Asp Thr 100 105 Lys Ile Gly Leu Gln Gln Lys Asn Ser Leu Leu Asp Trp Ile Asn Lys Ser Ile

<210> 137

130

<211> 106

<212> PRT

<213> Streptomyces aureofaciens

<400> 137

Gly Ala Thr Val Lys Val Thr Asn Ala Thr Phe Lys Ser Asp Val Leu Glu Ser Asp Lys Pro Val Leu Val His Phe Glu Gly Pro Trp Cys Gly 20 Pro Cys Lys Met Val Ala Pro Val Leu Asp Glu Ile Ala Asn Glu Tyr 40 Glu Gly Lys Val Lys Val Ala Lys Val Asn Thr Asp Glu Asn Pro Gln 55 60 Leu Ala Ser Gln Tyr Gly Val Arg Ser Ile Pro Thr Arg Leu Met Phe 70 Lys Gly Glu Val Ala Ala Asn Met Val Gly Ala Ala Pro Lys Thr 85 Arg Leu Ala Ala Phe Leu Asp Ala Ser Leu

<210> 138

<211> 110

<212> PRT

## <213> Streptomyces coelicolor

<210> 139 <211> 107

<212> PRT
<213> Streptomyces clavuligerus

<400> 139

 Met Ala Gly Val
 Leu Lys
 Asn Val
 Thr Asp Asp Thr Phe Glu Ala Asp 10
 15

 Val
 Leu Lys
 Ser Glu Lys
 Pro Val
 Leu Val
 Asp Phe Trp Ala Glu Trp 30

 Cys
 Gly Pro Cys
 Arg Gln Ile Ala Pro Ser Leu Glu Ala Ile Thr Glu 45

 His Gly Gly Gln Ile Glu Ile Val
 Lys
 Leu Asn Ile Asp Gln Asn Pro 50

 Ala Thr Ala Ala Lys
 Tyr Gly Val
 Met Ser Ile Pro Thr Leu Asn Val 65

 Tyr Gln Gly Glu Val
 Val
 Lys
 Thr Ile Val
 Gly Ala Lys
 Pro Lys 90

 Ala Ala Leu Leu Arg Pro Gly Pro Val
 Pro Arg 105

<210> 140 <211> 106 <212> PRT <213> Synechocystis

Thr Leu Ala Ser Thr Leu Glu Lys Tyr Leu 100 105

<210> 141 <211> 109 <212> PRT

<213> Synechocystis

<400> 141 Met Ser Leu Leu Glu Ile Thr Asp Ala Glu Phe Glu Gln Glu Thr Gln 10 Gly Gln Thr Lys Pro Val Leu Val Tyr Phe Trp Ala Ser Trp Cys Gly Pro Cys Arg Leu Met Ala Pro Ala Ile Gln Ala Ile Ala Lys Asp Tyr 35 40 Gly Asp Lys Leu Lys Val Leu Lys Leu Glu Val Asp Pro Asn Pro Ala 55 Ala Val Ala Gln Cys Lys Val Glu Gly Val Pro Ala Leu Arg Leu Phe 70 75 Lys Asn Asn Glu Leu Val Met Thr His Glu Gly Ala Ile Ala Lys Pro 85 90 Lys Leu Leu Glu Leu Leu Lys Glu Glu Leu Asp Phe Ile 100 105

<210> 142 <211> 108 <212> PRT

<213> Thiobacillus ferrooxidans

65 70 75 80
Leu Phe Lys Ala Gly Lys Leu Glu Ala Thr Lys Val Gly Ala Leu Ser
85 90 95

Lys Ala Gln Leu Thr Ala Phe Leu Asp Ser Gln Leu 100 105

<210> 143 <211> 91 <212> PRT

<213> Thiocapsa roseopersicina

<400> 143
Met Ser Asp Ser Ile Val His Val Thr Asp Asp Ser Phe Glu Asp Glu
1
Val Leu Lys Ser Leu Glu Pro Val Leu Val Asp Tyr Trp Ala Asp Trp
20
Cys Gly Pro Cys Lys Met Ile Ala Pro Val Leu Asp Glu Ile Ala Gly
35
Glu Tyr Ala Gly Arg Ile Lys Val Ala Lys Leu Asn Ile Asp Glu Asn
50
Pro Asn Thr Pro Arg Arg Tyr Gly Ile Arg Gly Ile Pro Thr Leu Met
65
Leu Ser Arg Gln Ser Glu Val Glu Ala Thr Lys
85

<210> 144 <211> 44 <212> PRT

<213> Tissierella creatinophila

<400> 144 Met Ile Glu Leu Asp Lys Ser Asn Phe Glu Glu Glu Val Leu Lys Ala 1 5 10 15

Glu Gly Thr Val Leu Val Asp Phe Trp Ser Pro Ser Cys Glu Pro Cys
20 25 30

Lys Ala Leu Met Pro His Val His Asp Phe Glu Glu
35 40

<210> 145

<211> 105

<212> PRT

<213> Treponema pallidum

<400> 145

Met Ala Leu Leu Asp Ile Ser Ser Gly Asn Val Arg Lys Thr Ile Glu 10 Thr Asn Pro Leu Val Ile Val Asp Phe Trp Ala Pro Trp Cys Gly Ser 20 25 30 Cys Lys Met Leu Gly Pro Val Leu Glu Glu Val Glu Ser Glu Val Gly 40 Ser Gly Val Val Ile Gly Lys Leu Asn Val Asp Asp Asp Gln Asp Leu 55 Ala Val Glu Phe Asn Val Ala Ser Ile Pro Thr Leu Ile Val Phe Lys 70 75 Asp Gly Lys Glu Val Asp Arg Ser Ile Gly Phe Val Asp Lys Ser Lys 85 90

Ile Leu Thr Leu Ile Gln Lys Asn Ala 100 105

<210> 146

<211> 104

<212> PRT

<213> Bos taurus

<400> 146

Val Lys Gln Ile Glu Ser Lys Tyr Ala Phe Gln Glu Ala Leu Asn Ser 10 Ala Gly Glu Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys Tyr 35 40 45 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val 55 Ala Ala Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 70 75 80 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 90 Glu Ala Thr Ile Asn Glu Leu Ile

<210> 147

<211> 166

<212> PRT

<213> Bos taurus

100

<400> 147

 Met Ala Gln Arg Leu Leu Leu Arg Arg Phe Leu Thr Ser Ile Ile Ser

 1
 5

 Gly Lys Pro Ser Gln Ser Arg Trp Ala Pro Val Ala Ser Arg Ala Leu

 20
 25

 Lys Thr Pro Gln Tyr Ser Pro Gly Tyr Leu Thr Val Thr Pro Ser Gln

 .35
 40

 Ala Arg Ser Ile Tyr Thr Thr Arg Val Cys Ser Thr Thr Phe Asn Ile

 50
 55

 60

 Gln Asp Gly Pro Asp Phe Gln Asp Arg Val Val Asn Ser Glu Thr Pro

 65
 70

 Val Val Val Val Asp Phe His Ala Gln Trp Cys Gly Pro Cys Lys Ile Leu

PCT/US01/50240 WO 02/50289

90 Gly Pro Arg Leu Glu Lys Val Val Ala Lys Gln His Gly Lys Val Val 110 100 105 Met Ala Lys Val Asp Ile Asp Asp His Thr Asp Leu Ala Leu Glu Tyr 120 125 115 Glu Val Ser Ala Val Pro Thr Val Leu Ala Met Lys Asn Gly Asp Val 135 140 Val Asp Lys Phe Val Gly Ile Lys Asp Glu Asp Gln Leu Glu Ala Phe 150 155 Leu Lys Lys Leu Ile Gly 165 <210> 148 <211> 115 <212> PRT <213> Caenorhabditis elegans <400> 148 Met Leu Lys Arg Cys Asn Phe Lys Asn Gln Val Lys Tyr Phe Gln Ser Asp Phe Glu Gln Leu Ile Arg Gln His Pro Glu Lys Ile Ile Leu

25 Asp Phe Tyr Ala Thr Trp Cys Gly Pro Cys Lys Ala Ile Ala Pro Leu 40 Tyr Lys Glu Leu Ala Thr Thr His Lys Gly Ile Ile Phe Cys Lys Val 55 Asp Val Asp Glu Ala Glu Asp Leu Cys Ser Lys Tyr Asp Val Lys Met 70 75 Met Pro Thr Phe Ile Phe Thr Lys Asn Gly Asp Ala Ile Glu Ala Leu 85 90 Glu Gly Cys Val Glu Asp Glu Leu Arg Gln Lys Val Leu Glu His Val 105 Ser Ala Gln

115

<210> 149 <211> 20 <212> PRT

<213> Canis familiaris

Val Lys Gln Ile Glu Phe Lys Tyr Ala Phe Gln Glu Ala Leu Asn Ser 1 Ala Gly Asp Lys 20

<210> 150 <211> 104 <212> PRT <213> Gallus gallus

<400> 150 Val Lys Ser Val Gly Asn Leu Ala Asp Phe Glu Ala Glu Leu Lys Ala 10 Ala Gly Glu Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 25 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Cys Asp Lys Phe 40 45 Gly Asp Val Val Phe Ile Glu Ile Asp Val Asp Asp Ala Gln Asp Val 55 Ala Thr His Cys Asp Val Lys Cys Met Pro Thr Phe Gln Phe Tyr Lys 75 Asn Gly Lys Lys Val Gln Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 90

Glu Glu Thr Ile Lys Ser Leu Val

<210> 151 <211> 107

<212> PRT

<213> Drosophila melanogaster

<400> 151

 Met Ala Ser Val
 Arg Thr Met Asn Asp Tyr His Lys Arg Ile Glu Ala

 1
 5

 Ala Asp Asp Lys Leu Ile Val Leu Asp Phe Tyr Ala Thr Trp Cys Gly

 20
 25

 20
 30

 Pro Cys Lys Glu Met Glu Ser Thr Val Lys Ser Leu Ala Arg Lys Tyr

 35
 40

 Ser Ser Lys Ala Val Val Leu Lys Ile Asp Val Asp Lys Phe Glu Glu

 50
 55

 Leu Thr Glu Arg Tyr Lys Val Arg Ser Met Pro Thr Phe Val Phe Leu

 65
 70

 Arg Gln Asn Arg Arg Leu Ala Ser Phe Ala Gly Ala Asp Glu His Lys

85 90 Leu Thr Asn Met Met Ala Lys Leu Val Lys Ala 100 105

<210> 152

<211> 104

<212> PRT

<213> Homo sapien

<400> 152

Glu Ala Thr Ile Asn Glu Leu Val 100

<210> 153

<211> 166

<212> PRT

<213> Homo sapien

<400> 153

 Met
 Ala
 Gln
 Arg
 Leu
 Leu
 Leu
 Arg
 Phe
 Leu
 Ala
 Ser
 Val
 Ile
 Ser

 Arg
 Lys
 Pro
 Ser
 Gln
 Trp
 Pro
 Pro
 Leu
 Thr
 Ser
 Lys
 Ala
 Leu

 Gln
 Thr
 Pro
 Gly
 Gly
 Leu
 Thr
 Val
 Thr
 Pro
 Asn
 Pro

 Ala
 Arg
 Thr
 Ile
 Thr
 Thr
 Thr
 Arg
 Ile
 Ser
 Leu
 Thr
 Val
 Thr
 Pro
 Asn
 Pro

 Ala
 Arg
 Thr
 Ile
 Thr
 Thr
 Thr
 Pro
 Asn
 Pro
 Asn
 Ile
 Ile
 Ile
 Asn
 <210> 154

<211> 104

<212> PRT

<213> Macaca mulatta

<400> 154

Val Lys Gln Ile Glu Ser Lys Ala Ala Phe Gln Glu Ala Leu Asp Asp Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 25 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys Tyr 35 40 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 70 75 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 90 Glu Ala Thr Ile Asn Glu Leu Val 100

<210> 155

<211> 104

<212> PRT

<213> Mus musculus

<400> 155

Val Lys Leu Ile Glu Ser Lys Glu Ala Phe Gln Glu Ala Leu Ala Ala Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 25 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Cys Asp Lys Tyr 35 40 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val Ala Ala Asp Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Tyr Lys 75 70 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 90 Glu Ala Ser Ile Thr Glu Tyr Ala 100

<210> 156

<211> 166

<212> PRT

<213> Mus musculus

<400> 156

 Met Ala Gln Arg Leu Leu Leu Gly Arg Phe Leu Thr Ser Val Ile Ser

 1
 5
 10
 15

 Arg Lys Pro Pro Gln Gly Val Trp Ala Ser Leu Thr Ser Lys Thr Leu
 20
 30

 Gln Thr Pro Gln Tyr Asn Ala Gly Gly Leu Thr Val Met Pro Ser Pro
 35
 40

Ala Arg Thr Val His Thr Thr Arg Val Cys Leu Thr Thr Phe Asn Val Gln Asp Gly Pro Asp Phe Gln Asp Arg Val Val Asn Ser Glu Thr Pro 70 75 Val Val Val Asp Phe His Ala Gln Trp Cys Gly Pro Cys Lys Ile Leu 85 90 95 Gly Pro Arg Leu Glu Lys Met Val Ala Lys Gln His Gly Lys Val Val 100 105 110 Met Ala Lys Val Asp Ile Asp Asp His Thr Asp Leu Ala Ile Glu Tyr 115 120 125 Glu Val Ser Ala Val Pro Thr Val Leu Ala Ile Lys Asn Gly Asp Val 135 140 Val Asp Lys Phe Val Gly Ile Lys Asp Glu Asp Gln Leu Glu Ala Phe 150 155 Leu Lys Lys Leu Ile Gly

<210> 157

<211> 33

<212> PRT

<213> Sus scrofa

<400> 157

Val Lys Gln Ile Glu Ser Lys Tyr Ala Phe Gln Glu Ala Leu Asn Ser 1 5 10 15 Ala Gly Glu Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 25 30 Pro

<210> 158

<211> 104

<212> PRT

<213> Oryctolagus cuniculus

<400> 158

Val Lys Gln Ile Glu Ser Lys Ser Ala Phe Gln Glu Val Leu Asp Ser 1 10 Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 25 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ala Leu Ser Glu Lys Phe 35 40 Asn Asn Val Val Phe Ile Glu Val Asp Val Asp Asp Cys Lys Asp Ile 55 60 Ala Ala Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 75 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 Glu Ala Thr Ile Asn Glu Leu Leu

100

<210> 159

<211> 104

<212> PRT

<213> Rattus norvegicus

<400> 159

```
55
                                            60
Ala Ala Asp Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Tyr Lys
                    70
                                        75
Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu .
                                    90
Glu Ala Thr Ile Thr Glu Phe Ala
<210> 160
```

<211> 166 <212> PRT <213> Rattus norvegicus

<400> 160 Met Ala Gln Arg Leu Leu Leu Arg Arg Phe Leu Thr Ser Val Ile Ser 10 Arg Lys Pro Pro Gln Gly Val Trp Ala Ser Leu Thr Ser Thr Ser Leu Gln Thr Pro Pro Tyr Asn Ala Gly Gly Leu Thr Gly Thr Pro Ser Pro 40 Ala Arg Thr Phe His Thr Thr Arg Val Cys Ser Thr Thr Phe Asn Val 55 60 Gln Asp Gly Pro Asp Phe Gln Asp Arg Val Val Asn Ser Glu Thr Pro Val Val Val Asp Phe His Ala Gln Trp Cys Gly Pro Cys Lys Ile Leu 90 85 Gly Pro Arg Leu Glu Lys Met Val Ala Lys Gln His Gly Lys Val Val 100 105 Met Ala Lys Val Asp Ile Asp Asp His Thr Asp Leu Ala Ile Glu Tyr 120 Glu Val Ser Ala Val Pro Thr Val Leu Ala Ile Lys Asn Gly Asp Val 135 140 Val Asp Lys Phe Val Gly Ile Lys Asp Glu Asp Gln Leu Glu Ala Phe 150 Leu Lys Lys Leu Ile Gly 165

<210> 161 <211> 104 <212> PRT

<213> Ovis aries

<400> 161 Val Lys Gln Ile Glu Ser Lys Tyr Ala Phe Gln Glu Ala Leu Asn Ser 10 Ala Gly Glu Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys Tyr 35 40 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val Ala Ala Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 70 75 Lys Gly Gln Lys Val Ser Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu

85 Glu Ala Thr Ile Asn Glu Leu Ile 100

<210> 162 <211> 261 <212> PRT <213> Arabidopsis thaliana <400> 162

```
Met Ala Arg Leu Val Phe Ser Leu Asn Leu Pro Ser Ser His Gly Phe
Asn Leu Ser Pro Arg Asn Leu Gln Ser Phe Phe Val Thr Gln Thr Gly
           20
Ala Pro Arg Phe Arg Ala Val Arg Cys Lys Pro Asn Pro Glu Ser Ser
                           40
Glu Thr Lys Gln Glu Lys Leu Val Ile Asp Asn Gly Glu Thr Ser Ser
                        55
                                            60
Ala Ser Lys Glu Val Glu Ser Ser Ser Ser Val Ala Asp Ser Ser Ser
                    70
Ser Ser Ser Ser Gly Phe Pro Glu Ser Pro Asn Lys Asp Ile Asn Arg
               85
                                    90
Arg Val Ala Ala Val Thr Val Ile Ala Ala Leu Ser Leu Phe Val Ser
           100
                                105
                                                    110
Thr Arg Leu Asp Phe Gly Ile Ser Leu Lys Asp Leu Thr Ala Ser Ala
                          120
Leu Pro Tyr Glu Glu Ala Leu Ser Asn Gly Lys Pro Thr Val Val Glu
                       135
                                            140
Phe Tyr Ala Asp Trp Cys Glu Val Cys Arg Glu Leu Ala Pro Asp Val
                    150
                                        155
Tyr Lys Ile Glu Gln Gln Tyr Lys Asp Lys Val Asn Phe Val Met Leu
                                    170
               165
Asn Val Asp Asn Thr Lys Trp Glu Gln Glu Leu Asp Glu Phe Gly Val
                                                   190
           180
                               185
Glu Gly Ile Pro His Phe Ala Phe Leu Asp Arg Glu Gly Asn Glu Glu
       195
                           200
                                               205
Gly Asn Val Val Gly Arg Leu Pro Arg Gln Tyr Leu Val Glu Asn Val
                        215
Asn Ala Leu Ala Ala Gly Lys Gln Ser Ile Pro Tyr Ala Arg Ala Val
                   230
                                       235
Gly Gln Tyr Ser Ser Ser Glu Ser Arg Lys Val His Gln Val Thr Asp
               245
                                    250
Pro Leu Ser His Gly
           260
```

<210> 163

<211> 140

<212> PRT

<213> Arabidopsis thaliana

<400> 163

Met Gly Ser Cys Val Ser Lys Gly Lys Gly Asp Asp Asp Ser Val His 10 Asn Val Glu Phe Ser Gly Gly Asn Val His Leu Ile Thr Thr Lys Glu 20 25 Ser Trp Asp Asp Lys Leu Ala Glu Ala Asp Arg Asp Gly Lys Ile Val 35 40 Val Ala Asn Phe Ser Ala Thr Trp Cys Gly Pro Cys Lys Ile Val Ala 55 Pro Phe Phe Ile Glu Leu Ser Glu Lys His Ser Ser Leu Met Phe Leu 75 70 Leu Val Asp Val Asp Glu Leu Ser Asp Phe Ser Ser Ser Trp Asp Ile 85 90 Lys Ala Thr Pro Thr Phe Phe Leu Lys Asn Gly Gln Gln Ile Gly 105 Lys Leu Val Gly Ala Asn Lys Pro Glu Leu Gln Lys Lys Val Thr Ser 115 120 Ile Ile Asp Ser Val Pro Glu Ser Pro Gln Arg Pro 130 135 140

<210> 164

<211> 186

<212> PRT

<213> Arabidopsis thaliana

```
<400> 164
Met Ser Glu Ile Val Asn Leu Ser Ser Ser Leu Arg Ser Leu Asn Pro
                                    10
Lys Ile Ser Pro Leu Val Pro Pro Tyr Arg Gln Thr Ser Ser Ser Phe
                                25
Ser Arg Pro Arg Asn Phe Lys Tyr His Ser Phe Thr Asp Lys Ile Cys
                            40
Leu Ala Ala Glu Arg Ile Arg Ala Val Asp Ile Gln Lys Gln Asp Gly
                        55
                                            60
Gly Leu Gln Glu Leu Asp Asp Ser Pro Val Ser Val Glu Leu Gly Pro
                    70
                                        75
Ile Cys Gly Glu Ser His Phe Asp Gln Val Met Glu Asp Ala Gln Lys
                85
                                   90
Leu Gly Glu Ser Val Val Ile Val Trp Met Ala Ala Trp Cys Arg Lys
           100
                                105
                                                   110
Cys Ile Tyr Leu Lys Pro Lys Leu Glu Lys Leu Ala Ala Glu Phe Tyr
       115
                            120
Pro Arg Leu Arg Phe Tyr His Val Asp Val Asn Ala Val Pro Tyr Arg
                        135
                                           140
Leu Val Ser Arg Ala Gly Val Thr Leu Trp Arg Asp Gly Gln Lys Gln
                    150
                                        155
Ala Glu Val Ile Gly Gly His Lys Ala His Phe Val Val Asn Glu Val
               165
                                    170
                                                        175
Arg Glu Met Ile Glu Asn Asp Ser Ile Thr
```

<210> 165

<211> 207

<212> PRT

<213> Arabidopsis thaliana

<400> 165

Met Glu Asn Met Ser Asn Leu Thr Ser Lys Phe Leu Leu Asn Pro Leu 10 Asn Val His Lys His Cys Ala Val Ser Asp Glu Asn Gly Asp Arg Lys 20 25 Ser His Val Leu Lys Gln Val Cys Ser Cys Ile Cys Cys Cys Asn Arg 40 Arg Asn Lys Thr Gln Ala Arg Ser Gln Lys Gly Ser Tyr Phe Ile Lys Gly Lys Val His Pro Val Ser Arg Met Glu Lys Trp Glu Glu Lys Ile 70 75 Thr Glu Ala Asn Ser His Gly Lys Ile Ile Ala Arg His Asp Leu Ile 90 Leu Cys Asn Met Glu Gln Leu Val Val Asn Phe Lys Ala Ser Trp Cys 105 Leu Pro Ser Lys Thr Ile Leu Pro Ile Tyr Gln Glu Leu Ala Ser Thr 120 125 Tyr Thr Ser Met Ile Phe Val Thr Ile Asp Val Glu Glu Leu Ala Ile 135 140 Ser Lys Leu Ser Asp Leu Gly Val Lys Ile Cys Leu Ile Gln Glu Phe 150 155 Ser His Glu Trp Asn Val Asp Ala Thr Pro Thr Val Val Phe Leu Lys 165 170 175 Asp Gly Arg Gln Met Asp Lys Leu Val Gly Gly Asp Ala Ala Glu Leu 180 185 190 Gln Lys Lys Thr Ala Ala Ala Ala Asn Leu Leu Leu Arg Gln Ser 200

<210> 166

<211> 175

<212> PRT

<213> Arabidopsis thaliana

<400> 166

```
Met Leu Ile Pro His Ala Val Ser Phe Ala Phe Thr Tyr Leu Arg Asn
Ser Ala Asn Pro Asp Gln Asn Arg Glu Val Ile Ser Ile His Ser Thr
                                25
           20
Ser Glu Leu Glu Ala Lys Thr Lys Ala Ala Lys Lys Ala Ser Arg Leu
                            40
                                                45
Leu Ile Leu Tyr Phe Thr Ala Thr Trp Cys Gly Pro Cys Arg Tyr Met
                        55
Ser Pro Leu Tyr Ser Asn Leu Ala Thr Gln His Ser Arg Val Val Phe
                    70
Leu Lys Val Asp Ile Asp Lys Ala Asn Asp Val Ala Ala Ser Trp Asn
                                    90
                85
Ile Ser Ser Val Pro Thr Phe Cys Phe Ile Arg Asp Gly Lys Glu Val
            100
                                105
Asp Lys Val Val Gly Ala Asp Lys Gly Ser Leu Glu Gln Lys Ile Ala
                            120
       115
Gln His Ser Ser Ser Lys Ala Arg Tyr Ile Pro Val Phe Ile Lys Tyr
                                            140
                       135
His Ser Asp Leu Leu Leu Val Asn Glu Glu Thr Pro Thr Ser Asn
                    150
                                        155
Gln Lys Leu Lys Thr Lys Thr Gly Asp Trp Phe His Ile Asn Leu
                                    170
```

<210> 167

<211> 132

<212> PRT

<213> Arabidopsis thaliana

<400> 167 Met Arg Lys Gln Glu Ser Glu Gly Ala Asn Leu Glu Phe Glu Ser Lys Ser Asn Asp Asn Gly Asn Val Lys Ile Ala Pro Asn Asp Gln Ser Phe 20 25 Leu Thr Ile Leu Asp Asp Ile Lys Ser Ser Lys Ser Pro Ala Val Ile Asn Tyr Gly Ala Ser Trp Tyr Thr Leu Phe Ser Val Phe Thr Ile Thr 55 60 Leu Phe Met Leu Ile Lys Cys Ser Met Lys Cys Leu Asn Glu Asn Gly 75 70 Phe Val Leu Lys Leu Ser Asp Ile Asp Glu Cys Pro Glu Thr Thr Arg 90 His Ile Arg Tyr Thr Pro Thr Phe Gln Phe Tyr Arg Asp Gly Glu Lys 105 Val Asp Glu Met Phe Gly Ala Gly Glu Gln Arg Leu His Asp Arg Leu 115 Trp Leu His Ser

<210> 168

130

<211> 151

<212> PRT

<213> Arabidopsis thaliana

```
85
Lys Ile Asp Thr Glu Lys Tyr Pro Ser Ile Ala Asn Lys Tyr Lys Ile
                          105
            100
Glu Ala Leu Pro Thr Phe Ile Leu Phe Lys Asp Gly Glu Pro Cys Asp
                           120
Arg Phe Glu Gly Ala Leu Thr Ala Lys Gln Leu Ile Gln Arg Ile Glu
                        135
Asp Ser Leu Lys Val Lys Pro
                    150
<210> 169
<211> 236
<212> PRT
<213> Arabidopsis thaliana
<400> 169
Met Ala Gly Val Val Arg Leu Thr Thr Ser Val Gln Ala Ile Arg
Val Ser Ser Ser Phe Ser Ser Phe Ala Thr Ala Leu Asn Pro Leu Gln
        20
                                25
Pro Cys Leu Pro Pro Asn Ser Asn Leu Asn Ser Asp Lys Arg Leu Arg
                            40
Leu Leu Ser Ser Ser Pro Ser Cys Ser Ser Ser His Tyr His Pro Ser
Ser Gly Leu Gly Ser His Leu Pro Leu Arg Arg Pro Lys Ser Gln Val
Val Arg Val Lys Val Asp Glu Asn Val Ala Glu Thr Glu Pro Pro Lys
                85
                                   90
Trp Trp Glu Arg Asn Ala Pro Asn Met Val Asp Ile His Ser Thr Glu
            100
                                105
Glu Phe Leu Ser Ala Leu Ser Gly Ala Gly Glu Arg Leu Val Ile Val
                            120
                                                125
Glu Phe Tyr Gly Thr Trp Cys Ala Ser Cys Arg Ala Leu Phe Pro Lys
                        135
                                           140
Leu Cys Lys Thr Ala Val Glu His Pro Asp Ile Val Phe Leu Lys Val
                    150
                                       155
Asn Phe Asp Glu Asn Lys Pro Met Cys Lys Ser Leu Asn Val Arg Val
               165
                                   170
Leu Pro Phe Phe His Phe Tyr Arg Gly Ala Asp Gly Gln Leu Glu Ser
                                185
                                                   190
Phe Ser Cys Ser Leu Ala Lys Val Lys Lys Ala Ile Ser Val Ser Pro
                           200
Phe Pro Gln Leu Glu Leu Gly Ile Thr Leu Gln Thr Lys Arg Thr Thr
                       215
Ser Leu Phe Phe Phe Asp Arg Ile Tyr Gln Ile Leu
                    230
<210> 170
<211> 131
<212> PRT
<213> Hordeum bulbosum
<400> 170
Met Gly Gly Cys Val Gly Lys Asp Arg Ser Ile Val Glu Asp Lys Leu
                                   10
Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp
           20
Asp Gln Lys Val Ala Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala
                           40
Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val
                        55
                                           60
Tyr Ala Glu Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile
                    70
                                       75
Asp Val Asp Asp Leu Met Asp Phe Gly Ser Thr Trp Asp Ile Arg Ala
```

```
Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Asp Lys Leu
                                 105
Val Gly Ala Asn Lys Pro Glu Leu Glu Lys Lys Val Gln Ala Leu Gly
        115
                            120
Asp Gly Ser
    130
<210> 171
<211> 131
<212> PRT
<213> Lolium perenne
<400> 171
Met Gly Gly Cys Val Gly Lys Asp Arg Ser Ile Val Glu Asp Lys Leu
                                    10
Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp
            20
                                25
Asp Gln Lys Val Ala Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala
        35
Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val
                        55
Tyr Ala Glu Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile
                    70
                                        75
Asp Val Asp Asp Leu Met Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala
                85
                                    90
Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Leu Ile Asp Lys Leu
                                105
Val Gly Ala Asn Arg Pro Glu Leu Glu Lys Lys Val Gln Ala Ile Gly
        115
Asp Gly Ser
   130
<210> 172
<211> 131
<212> PRT
<213> Oryza sativa
<400> 172
Met Gly Ser Cys Val Gly Lys Glu Arg Ser Asp Glu Glu Asp Lys Ile
                                    1.0
Asp Phe Lys Gly Gly Asn Val His Val Ile Ser Asn Lys Glu Asn Trp
Asp His Lys Ile Ala Glu Ala Asn Lys Asp Gly Lys Ile Val Ile Ala
        35
                            40
                                               . 45
Asn Phe Ser Ala Ala Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val
                        55
                                            60
Tyr Ala Glu Met Ser Gln Thr Tyr Pro Gln Phe Met Phe Leu Thr Ile
                    70
                                        75
Asp Val Asp Glu Leu Met Asp Phe Ser Ser Ser Trp Asp Ile Arg Ala
                85
                                    90
Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Glu Gln Val Asp Lys Leu
                                105
                                                    110
            100
Val Gly Ala Asn Lys Pro Glu Leu Glu Lys Lys Val Ala Ala Leu Ala
        115
                            120
Asp Ser Ala
   130
<210> 173
<211> 296
<212> PRT
<213> Solanum tuberosum
<400> 173
```

Met Ala Thr Leu Thr Asn Phe Leu Leu Lys Pro Ser Pro Asn Leu Ala

```
Ser Ile Thr Lys Ile Ser Pro Ser Leu Tyr Ser Asn Phe Pro Phe Glu
                             25
Lys Ser Lys Gln Ser Ile Phe Lys Asn Leu Lys Thr Asn Lys Pro Leu
                          40
Leu Ile Thr Lys Ala Thr Ala Ala Pro Asp Val Glu Lys Lys Val Ala
Lys Ser Glu Arg Val Gln Lys Val Asn Ser Met Glu Glu Leu Asp Glu
Ala Leu Lys Lys Ala Lys Asn Arg Leu Val Val Glu Phe Ala Gly
               85
                                   90
Lys Asp Ser Glu Arg Ser Lys Asn Ile Tyr Pro Phe Met Val Asn Leu
           100
                               105
Ser Lys Thr Cys Asn Asp Val Asp Phe Leu Leu Val Ile Gly Asp Glu
                           120
Thr Glu Lys Thr Lys Ala Leu Cys Arg Arg Glu Lys Ile Asp Lys Val
                     135
                                           140
Pro His Phe Asn Phe Tyr Lys Ser Met Glu Lys Ile His Glu Glu Glu
                   150
                                       155
Gly Ile Gly Pro Asp Leu Leu Ala Gly Asp Val Leu Tyr Tyr Gly Asp
                                   170
Ser His Ser Glu Val Val Gln Leu His Ser Arg Glu Asp Val Glu Lys
                               185
           180
Val Ile Gln Asp His Lys Ile Asp Lys Lys Leu Ile Val Leu Asp Val
       195
                           200
                                               205
Gly Leu Lys His Cys Gly Pro Cys Val Lys Val Tyr Pro Thr Val Ile
                       215
                                           220
Lys Leu Ser Lys Gln Met Ala Asp Thr Val Val Phe Ala Arg Met Asn
                   230
                                       235
Gly Asp Glu Asn Asp Ser Cys Met Gln Phe Leu Lys Asp Met Asp Val
                245
                                   250
Ile Glu Val Pro Thr Phe Leu Phe Ile Arg Asp Gly Glu Ile Cys Gly
                               265
                                                   270
Arg Tyr Val Gly Ser Gly Lys Gly Glu Leu Ile Gly Glu Ile Leu Arg
Tyr Gln Gly Val Arg Val Thr Tyr
```

<210> 174 <211> 131 <212> PRT

<213> Secale cereale

<400> 174 Met Gly Gly Cys Val Gly Lys Gly Arg Ser Ile Val Glu Glu Lys Leu 10 Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp Asp Gln Lys Ile Glu Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala 35 45 40 Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Val Ala Pro Val 55 Tyr Ala Gly Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile 70 Asp Val Asp Asp Leu Met Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala 90 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Asp Lys Leu 1.00 105 110 Val Gly Ala Asn Lys Pro Glu Leu Glu Lys Lys Val Gln Ala Leu Gly 115 Asp Gly Ser 130

<210> 175 <211> 119

<212> PRT <213> Secale cereale

<400> 175 Met Gly Gly Cys Val Gly Lys Gly Arg Ser Ile Val Glu Glu Lys Leu 10 Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp 20 25 Asp Gln Lys Ile Glu Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala 35 40 45 Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val Tyr Ala Glu Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile 70 Asp Val Asp Asp Leu Met Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala 90 85 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Asp Lys Leu 105 110 Val Gly Ala Asn Lys Pro Glu 115

<210> 176 <211> 106 <212> PRT

<213> Manduca sexta

<210> 177 <211> 221 <212> PRT <213> Bradyrhizobium japonicum

<400> 177 Met Leu Asp Thr Lys Pro Ser Ala Thr Arg Arg Ile Pro Leu Val Ile 10 Ala Thr Val Ala Val Gly Gly Leu Ala Gly Phe Ala Ala Leu Tyr Gly 25 Leu Gly Leu Ser Arg Ala Pro Thr Gly Asp Pro Ala Cys Arg Ala Ala 35 40 Val Ala Thr Ala Gln Lys Ile Ala Pro Leu Ala His Gly Glu Val Ala 60 50 Ala Leu Thr Met Ala Ser Ala Pro Leu Lys Leu Pro Asp Leu Ala Phe 75 Glu Asp Ala Asp Gly Lys Pro Lys Lys Leu Ser Asp Phe Arg Gly Lys 90 Thr Leu Leu Val Asn Leu Trp Ala Thr Trp Cys Val Pro Cys Arg Lys 105 110 Glu Met Pro Ala Leu Asp Glu Leu Gln Gly Lys Leu Ser Gly Pro Asn 125 120 Phe Glu Val Val Ala Ile Asn Ile Asp Thr Arg Asp Pro Glu Lys Pro

```
130
                       135
Lys Thr Phe Leu Lys Glu Ala Asn Leu Thr Arg Leu Gly Tyr Phe Asn
              150
                                    155
Asp Gln Lys Ala Lys Val Phe Gln Asp Leu Lys Ala Ile Gly Arg Ala
                                  170
                                                      175
               165
Leu Gly Met Pro Thr Ser Val Leu Val Asp Pro Gln Gly Cys Glu Ile
                                                  190
                               185
Ala Thr Ile Ala Gly Pro Ala Glu Trp Ala Ser Glu Asp Ala Leu Lys
                           200
Leu Ile Arg Ala Ala Thr Gly Lys Ala Ala Ala Leu
                       215
```

<210> 178

<211> 167

<212> PRT

<213> Haemophilus influenzae

<400> 178 Met Lys Ile Lys Lys Leu Leu Lys Asn Gly Leu Ser Leu Phe Leu Thr Phe Ile Val Ile Thr Ser Ile Leu Asp Phe Val Arg Arg Pro Val Val 25 Pro Glu Glu Ile Asn Lys Ile Thr Leu Gln Asp Leu Gln Gly Asn Thr 35 40 Phe Ser Leu Glu Ser Leu Asp Gln Asn Lys Pro Thr Leu Leu Tyr Phe Trp Gly Thr Trp Cys Gly Tyr Cys Arg Tyr Thr Ser Pro Ala Ile Asn 70 75 Ser Leu Ala Lys Glu Gly Tyr Gln Val Val Ser Val Ala Leu Arg Ser 90 85 Gly Asn Glu Ala Asp Val Asn Asp Tyr Leu Ser Lys Asn Asp Tyr His 105 Phe Thr Thr Val Asn Asp Pro Lys Gly Glu Phe Ala Glu Arg Trp Gln 115 120 125 Ile Asn Val Thr Pro Thr Ile Val Leu Leu Ser Lys Gly Lys Met Asp 135 140 Leu Val Thr Thr Gly Leu Thr Ser Tyr Trp Gly Leu Lys Val Arg Leu 155 150 Phe Phe Ala Glu Phe Phe Gly

<210> 179

<211> 163

<212> PRT

<213> Leishmania major

165

<400> 179

Met Leu Lys Val Ser Ser Lys Glu His Tyr Ala Glu Ile Lys Lys 10 Ala Glu Asp Ser Leu Gly Leu Val Val His Phe Ser Ala Thr Trp Cys Glu Pro Cys Thr Ala Val Asn Glu His Leu Thr Lys Gln Ala Ala Glu 45 40 Tyr Gly Asp Asn Val Val Phe Ala Glu Val Asp Cys Gly Glu Leu Gly 55 Asp Val Cys Glu Ala Glu Gly Val Glu Ser Val Pro Phe Val Ala Tyr 70 75 Phe Arg Thr Pro Leu Val Gly Asp Asp Arg Arg Val Glu Arg Val Ala 85 90 Asp Val Ala Gly Ala Lys Phe Asp Gln Ile Asp Met Asn Thr His Ser 105 Leu Phe Gly Glu Lys Gly Gly Asn Arg Gly Ser Ala Glu Gly Leu Cys 125 120 His Ser Gly Arg Leu Pro Ala Leu Pro His Glu Ala Ala Arg Gly Arg 130 135

Asn Val His His Arg His Pro Ile Ser Ser Ala Leu Arg Leu Tyr Trp 150 Ser Ala Val

<210> 180

<211> 275

<212> PRT

<213> Mortierella alpina

<400> 180 Met Val Ser Asn Asn Tyr Ile Asp Ile Thr Ser Glu Asp Asp Phe Ala 10 Gln Val Phe Gln Pro Ser Ser Ser Thr Val Tyr Ala Leu Asn Phe Trp 25 Ala Ala Trp Ala Pro Pro Cys Val Gln Met Asn Glu Val Phe Glu Glu 35 40 Leu Ala Ala Lys Asn Ala Asn Val Asn Phe Leu Lys Ile Glu Ala Glu 55 Lys Phe Pro Asp Ile Ser Glu Asp Tyr Glu Ile Ala Ala Val Pro Ser 75 70 Phe Val Ile Val Lys Glu Gly Thr Val Val Asp Arg Val Glu Gly Ala 90 Asn Ala Pro Glu Leu Ala Lys Val Ile Ala Lys Tyr Ser Lys Ser Thr 105 110 Ser Ser Pro Leu Pro Thr Gln Ser Ser Thr Met Ala Ala Ala Gly His 115 120 125 Ala Ala Pro Ser Val Ala Pro Pro Thr Met Ser Pro Glu Glu Met Asn 140 135 Ala Arg Leu Lys Glu Leu Thr Ser Ser Ser Ser Val Met Ala Phe Ile 150 155 Lys Gly Thr Pro Thr Ala Pro Arg Cys Gln Phe Ser Arg Gln Leu Leu 170 165 175 Glu Ile Leu Thr Ala Gln Asn Ile Arg Phe Ser Ser Phe Asn Ile Leu 190 180 185 Ala Asp Asp Glu Val Arg Gln Ala Met Lys Thr Phe Ser Asp Trp Pro 195 200 Thr Phe Pro Gln Val Tyr Val Lys Gly Glu Phe Val Gly Gly Leu Asp 21.5 Val Val Lys Glu Leu Val Ala Ser Gly Glu Phe Gln Ala Leu Val Pro 230 235 Ala Glu Lys Asp Leu Lys Thr Arg Met Asp Glu Leu Ile Arg Lys Ala . 250 245 255 Pro Val Met Ile Phe Ile Lys Gly Ser Pro Glu Thr Pro Arg Cys Gly

<210> 181

Phe Ser Lys

275

<211> 160

<212> PRT

<213> Neisseria gonorrhoeae

<400> 181

Met Lys Arg'Leu Ile Leu Ala Ala Ile Ala Leu Ala Ala Thr Phe Gly Ala His Thr Ala Ser Gly Asp Glu Leu Ala Gly Trp Lys Asp Asn Thr Pro Gln Asn Leu Gln Ser Leu Lys Ala Pro Val Arg Ile Ala Asn Leu 40 Trp Ala Thr Trp Cys Gly Pro Cys Arg Lys Glu Met Pro Ala Met Ser Lys Trp Tyr Lys Ala Gln Lys Lys Gly Ser Val Asp Met Val Gly Ile 70 75 Ala Leu Asp Thr Ser Asp Asn Ile Gly Asn Phe Leu Lys Gln Thr Pro

 Val
 Ser
 Tyr
 Pro
 Ile
 Trp
 Arg
 Tyr
 Thr
 Gly
 Ala
 Asn
 Ser
 Arg
 Ser
 Phe

 Met
 Lys
 Ser
 Tyr
 Gly
 Asn
 Asn
 Val
 Gly
 Val
 Leu
 Pro
 Phe
 Thr
 Val
 Val

 Glu
 Ala
 Pro
 Lys
 Cys
 Gly
 Tyr
 Arg
 Gln
 Thr
 Ile
 Thr
 Gly
 Glu
 Leu
 Asn

 130
 135
 135
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 140
 1

<210> 182 <211> 208

<212> PRT

<213> Rhizobium loti

<400> 182 Met Ala Gly Ala Leu Ala Gly Ala Val Ala Val Tyr Val Ser Glu Ser Arg Ser Gly Asn Asn Ala Pro Ala Arg Val Ala Val Gly Gly Ser Lys 20 Asp Asp Val Ala Cys Ala Ala Lys Ser Gly Arg Ala Lys Lys Ile Ala 40 Ala Ala Thr Gly Glu Val Ala Ala Leu Leu Pro Ala Asp Pro Pro Gln Ser Met Lys Ser Leu Ala Phe Asn Gly Pro Asp Gly Lys Pro Met 70 75 Thr Ile Ala Asp His Ala Gly Lys Thr Val Leu Leu Asn Leu Trp Ala 85 90 Thr Trp Cys Ala Pro Cys Arg Ala Glu Met Pro Ala Leu Asn Ala Leu 100 105 110 Gln Lys Asp Lys Gly Ser Asp Ala Phe Gln Val Ile Ala Val Asn Val 125 115 120 Asp Ala Gly Asp Asp Val Lys Pro Lys Lys Phe Leu Lys Glu Thr Gly 135 130 140 Val Glu Ala Leu Gly Tyr Phe Arg Asp Ser Thr Val Ala Leu Phe Asn 150 155 Asp Leu Lys Ala Arg Gly Leu Ala Leu Gly Leu Pro Val Thr Met Leu 165 170 Ile Asp Ser Glu Gly Cys Leu Ile Ala His Met Asn Gly Pro Ala Glu 180 185 Trp Ser Gly Arg Asp Ala Arg Arg Leu Val Glu Thr Ala Leu Gly Ser 200

<210> 183

<211> 176

<212> PRT

<213> Rhodobacter capsulatus

<400> 183

Met Ala Lys Pro Leu Met Phe Leu Pro Leu Val Met Ala Gly Phe 10 Val Gly Ala Gly Tyr Phe Ala Met Gln Gln Asn Asp Pro Asn Ala Met 20 Pro Thr Ala Leu Ala Gly Lys Glu Ala Pro Ala Val Arg Leu Glu Pro 35 40 Leu Gly Ala Glu Ala Pro Phe Thr Asp Ala Asp Leu Arg Asp Gly Lys 55 Ile Lys Leu Val Asn Phe Trp Ala Ser Trp Cys Ala Pro Cys Arg Val Glu His Pro Asn Leu Ile Gly Leu Lys Gln Asp Gly Ile Glu Ile Met 85 90 Gly Val Asn Trp Lys Asp Thr Pro Asp Gln Ala Gln Gly Phe Leu Ala 105 100 Glu Met Gly Ser Pro Tyr Thr Arg Leu Gly Ala Asp Pro Gly Asn Lys 120

<210> 184

<211> 105

<212> PRT

<213> Synechocystis

<400> 184

Met Ala Val Lys Lys Gln Phe Ala Asn Phe Ala Glu Met Leu Ala Gly 10 Ser Pro Lys Pro Val Leu Val Asp Phe Tyr Ala Thr Trp Cys Gly Pro 30 25 20 Cys Gln Met Met Ala Pro Ile Leu Glu Gln Val Gly Ser His Leu Arg 40 Gln Gln Ile Gln Val Val Lys Ile Asp Thr Asp Lys Tyr Pro Ala Ile 55 Ala Thr Gln Tyr Gln Ile Gln Ser Leu Pro Thr Leu Val Leu Phe Lys 75 Gln Gly Gln Pro Val His Arg Met Glu Gly Val Gln Gln Ala Ala Gln 85 90 Leu Ile Gln Gln Leu Gln Val Phe Val 100

<210> 185

<211> 109

<212> PRT

<213> Synechocystis

<400> 185

Met Ser Leu Leu Glu Ile Thr Asp Ala Glu Phe Glu Glu Glu Thr Gln 10 Gly Gln Thr Lys Pro Val Leu Val Tyr Phe Trp Ala Ser Trp Cys Gly 20 25 30 Pro Cys Arg Leu Met Ala Pro Ala Ile Gln Ala Ile Ala Lys Asp Tyr Gly Asp Lys Leu Lys Val Leu Lys Leu Glu Val Asp Pro Asn Pro Ala 60 55 Ala Val Ala Gln Cys Lys Val Glu Gly Val Pro Ala Leu Arg Leu Phe 70 Lys Asn Asn Glu Leu Val Met Thr His Glu Gly Ala Ile Ala Lys Pro 90 Lys Leu Leu Glu Leu Leu Lys Glu Glu Leu Asp Phe Ile 100

<210> 186

<211> 290

<212> PRT

<213> Schizosaccharomyces pombe

<400> 186

 Met
 Ser
 Val
 Ile
 Glu
 Ile
 Arg
 Ser
 Tyr
 Gln
 His
 Trp
 Ile
 Ser
 Thr
 Ile

 Pro
 Lys
 Ser
 Gly
 Tyr
 Leu
 Ala
 Val
 Asp
 Cys
 Tyr
 Ala
 Asp
 Trp
 Cys
 Gly

 Pro
 Cys
 Lys
 Ala
 Ile
 Ser
 Pro
 Leu
 Phe
 Ser
 Gln
 Leu
 Ala
 Ser
 Lys
 Tyr

 Ala
 Ser
 Pro
 Lys
 Phe
 Ala
 Lys
 Val
 Asn
 Val
 Asp
 Glu
 Gln
 Arg

 Gln
 Ile
 Ala
 Ser
 Gly
 Leu
 Gly
 Val
 Lys
 Ala
 Met
 Pro
 Thr
 Phe
 Val
 Phe

```
70
Phe Glu Asn Gly Lys Gln Ile Asp Met Leu Thr Gly Ala Asn Pro Gln
                85
                                   90
Ala Leu Lys Glu Lys Val Ala Leu Ile Ser Ser Lys Ala Thr Gly Thr
                               105
           100
Gly Ala Leu Ala Ser Ser Ser Ser Ala Pro Val Lys Gly Phe Ala Ser
                                               125
                           120
Leu Gln Gly Cys Ile Glu Asn Pro Gln Leu Glu Cys Leu Asn Gln Gln
                        135
Asp Asp His Asp Leu Lys Ser Ala Phe Asn Ser Asn Pro Ser Ser Phe
                                      155
                   150
Leu Glu Ser Asp Val Asp Glu Gln Leu Met Ile Tyr Ile Pro Phe Leu
               165
                                   170
Glu Val Val Lys Val His Ser Ile Ala Ile Thr Pro Val Lys Gly Glu
                               185
                                                   190
Thr Ser Ser Ala Pro Lys Thr Ile Lys Leu Tyr Ile Asn Gln Pro Asn
                                               205
                           200
Asn Leu Ser Phe Glu Asp Ala Glu Ser Phe Thr Pro Thr Gln Val Ile
                                          220
                        215
Glu Asp Ile Val Tyr Glu Gln Asp Asp Gln Pro Thr Ile Ile Pro Leu
                    230
                                       235
Arg Phe Val Lys Phe Gln Arg Val Asn Ser Leu Val Ile Phe Ile Tyr
                                 250
               245
Ser Asn Val Gly Glu Glu Glu Thr Thr Lys Ile Ser Arg Leu Glu Leu
                               265
                                                   270
           260
Phe Gly Glu Pro Val Gly Asp Ser Ser Lys Gly Lys Leu Gln Lys Val
                            280
Glu Ala
   290
```

<210> 187

<211> 185

<212> PRT

<213> Treponema pallidum

<400> 187

Met Phe Arg Ser Asp Leu Val Leu Ala Val Trp Gly Val Thr Cys Val 10 Gln Ala Ala Asp Val Ala His Asn Ala Asp Val Pro Ser Arg Ser Leu 25 Lys Ala Leu Glu Arg Phe Arg Phe Phe Val Tyr Pro Lys Pro Leu Asp 35 40 Leu Ser Ser Asp Phe His Ala Lys Ala Leu Lys Gly Glu Ala Leu Val Pro Ser Leu Phe Lys Gly Lys Val Thr Leu Leu Asn Phe Trp Ala Thr 75 70 Trp Cys Pro Pro Cys Arg Ala Glu Met Pro Ser Met Asp Arg Met Gln 85 Ala Leu Met Arg Gly Asn Asp Phe Gln Ile Val Ala Val Asn Val Gly 105 Asp Ser Arg Lys Gln Val Glu Ser Phe Ile Ala Arg Gly Lys His Thr 125 115 120 Phe Pro Ile Tyr Leu Asp Glu Glu Gly Ser Leu Gly Ser Val Phe Ala 135 140 Ser Arg Gly Leu Pro Thr Thr Tyr Val Val Asp Lys Ala Gly, Arg Ile 150 Val Ala Val Val Gly Ser Val Glu Tyr Asp Gln Pro Glu Leu Val 165 170 Ala Leu Phe Lys Glu Leu Ala Arg Asp 180

<210> 188

<211> 246

<212> PRT

<213> Caenorhabditis elegans

<400> 188 Met Leu Leu Arg Leu Leu Ala Val Leu Gly Leu Phe Ala Val Gly Val 10 Ser Gly Gly Pro Thr Arg Ser Ser Lys Leu Val Phe Leu Asn Glu Glu 25 Asn Trp Thr Asp Leu Met Lys Gly Glu Trp Met Ile Glu Phe His Ala 40 Pro Trp Cys Pro Ala Cys Lys Asp Leu Gln Lys Ala Trp Asn Ala Phe 55 Ala Asp Trp Ser Asp Asp Leu Gly Ile Lys Val Gly Glu Val Asp Val 70 75 Thr Val Asn Pro Gly Leu Ser Gly Arg Phe Leu Val Thr Ala Leu Pro 85 90 Thr Ile Tyr His Val Lys Asp Gly Val Phe Arg Gln Tyr Ser Gly Ala 105 100 Arg Asp Lys Asn Asp Phe Ile Ser Phe Val Glu Asp Lys Lys Tyr Arg 125 115 120 Val Ile Asp Pro Val Pro Asp Tyr Lys His Pro Asn Ser Lys Gln Met 135 140 Ala Val Val Ala Val Phe Phe Lys Leu Ser Met Ser Val Arg Asp Leu 155 150 His Asn His Leu Val Glu Asp Lys Gly Ile Pro Ser Trp Ala Ser Tyr 170 175 165 Gly Leu Phe Ala Gly Val Thr Leu Ala Leu Gly Cys Val Leu Gly Phe 180 185 190 Phe Ile Val Ile Ile Ile Asp Gln Val Phe Pro Thr Gly Pro Arg Lys 205 200 Ser Gln Gln Ala Lys Lys Thr Glu Lys Lys Asp Ala Lys Lys Asp Ser 215 220 Gly Thr Glu Ser Pro Thr Lys Lys Asn Gly Asn Asn Asn Asn Gly Lys 230 235 Glu Thr Lys Lys Thr Lys

<210> 189 <211> 284 <212> PRT

<213> Caenorhabditis elegans

<400> 189 Met Pro Val Ile Asn Val Lys Asp Asp Glu Asp Phe Arg Asn Gln Leu 10 Ser Leu Ala Gly Leu Lys Ser Val Ile Val Asp Phe Thr Ala Val Trp 20. 25 , Cys Gly Pro Cys Lys Met Ile Ala Pro Thr Phe Glu Ala Leu Ser Asn 40 Gln Tyr Leu Gly Ala Val Phe Leu Lys Val Asp Val Glu Ile Cys Glu 55 Lys Thr Ser Ser Glu Asn Gly Val Asn Ser Met Pro Thr Phe Met Val 75 70 Phe Gln Ser Gly Val Arg Val Glu Gln Met Lys Gly Ala Asp Ala Lys 85 Ala Leu Glu Thr Met Val Lys Lys Tyr Ala Asp Asn Ser Ala Ala Asp 105 Ser Leu Val Ala Gly Gln Met Asp Leu Thr Pro Leu Val Asp Lys Lys 115 120 125 Gln Met Glu Cys Leu Asn Glu Ser Asp Asp Thr Pro Leu Gly Arg Phe 130 135 140 Leu Glu Gly Asn Cys Asn Leu Val Ser Asp Cys Asp Glu Gln Leu Ile 150 · 155 Ile Ser Leu Pro Phe Asn Gln Pro Val Lys Val His Ser Ile Leu Ile 165 170 Lys Gly Val Ser Asp Arg Ala Pro Lys Lys Val Lys Val Phe Ile Asn 190 180 185 Leu Pro Lys Thr Thr Asp Phe Asp Asn Ala Thr Ala Leu Glu Pro Thr 200

Gln Met Leu Glu Phe Asp Glu Ser Ser Ile Gln Gly His Gly Gln Val
210

Val Ala Leu Lys Tyr Val Lys Phe Gln Asn Val Gln Asn Ile Gln Phe
225

Phe Ile Glu Asn Asn Val Gly Gly Gly Asp Val Thr Glu Leu Val Lys
245

Leu Thr Val Phe Gly Thr Pro Leu Ser Ala Leu Asn Met Asn Glu Phe
260

Lys Arg Val Ala Gly Lys Ala Gly Asp Ala Ala His
275

<210> 190 <211> 287 <212> PRT <213> Drosophila melanogaster

<400> 190 Met Ser Val Arg Val Ile Asn Asp Glu Ser His Phe Gln Ala Glu Leu 10 Ala Gln Ala Gly Ile Gln Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Lys Arg Ile Ala Pro Ile Phe Glu Thr Phe Pro Thr 35 40 Lys Tyr Pro Lys Ala Ile Phe Leu Lys Val Asp Val Asp Lys Cys Gln 55 60 Asp Thr Ala Ala Gly Gln Gly Val Ser Ala Met Pro Thr Phe Ile Phe 70 75 Tyr Arg Asn Arg Thr Lys Ile Asp Arg Val Gln Gly Ala Asp Val Asn 90 Gly Leu Glu Ala Lys Ile Gln Glu His Ile Gly Thr Ser Gly Glu Glu 105 110 100 Glu Gly Gly Glu Asp Tyr Gly Gln Gly Leu Met Glu Leu Asn Thr Phe 115 120 125 Ile Ser Lys Gln Glu Cys Glu Cys Leu Asn Glu Ala Asp Asp His Asn 135 Leu Lys His Ala Leu Ala Ser Ala Gly Gly Tyr Leu Gln Ser Asp Cys 150 155 Asp Glu Gln Leu Ile Leu Ser Ile Thr Phe Asn Gln Ala Val Lys Ile 170 175 165 His Ser Leu Lys Phe Lys Ala Pro Ser His Leu Gly Pro Lys Asp Val 190 180 185 Lys Leu Phe Il'e Asn Gln Pro Arg Thr Ile Asp Phe Asp Met Ala Glu 200 205 195 Ser Met Asn Ser Val Gln Asp Leu Ser Leu Ala Gln Lys Glu Leu Glu 215 220 Ser Gly Val Pro Val Asn Leu Arg Tyr Val Lys Phe Gln Asn Val Gln 235 230 Asn Ile Gln Ile Phe Val Lys Asn Asn Gln Ser Gly Gly Asp Val Thr 245 250 Gln Ile Asp Tyr Ile Gly Phe Ile Gly Ser Pro Ile Met Thr Thr Lys 260 265 Met Asn Asp Phe Lys Arg Val Ala Gly Lys Lys Gly Glu Ser His 280

<210> 191 <211> 289 <212> PRT

<213> Homo sapien

40 Asn Lys Tyr Pro Gln Ala Val Phe Leu Glu Val Asp Val His Gln Cys 55 Gln Gly Thr Ala Ala Thr Asn Asn Ile Ser Ala Thr Pro Thr Phe Leu 70 Phe Phe Arg Asn Lys Val Arg Ile Asp Gln Tyr Gln Gly Ala Asp Ala 85 90 Val Gly Leu Glu Glu Lys Ile Lys Gln His Leu Glu Asn Asp Pro Gly 105 Ser Asn Glu Asp Thr Asp Ile Pro Lys Gly Tyr Met Asp Leu Met Pro 120 125 Phe Ile Asn Lys Ala Gly Cys Glu Cys Leu Asn Glu Ser Asp Glu His 135 140 Gly Phe Asp Asn Cys Leu Arg Lys Asp Thr Thr Phe Leu Glu Ser Asp 150 155 Cys Asp Glu Gln Leu Leu Ile Thr Val Ala Phe Asn Gln Pro Val Lys 165 170 Leu Tyr Ser Met Lys Phe Gln Gly Pro Asp Asn Gly Gln Gly Pro Lys 185 Tyr Val Lys Ile Phe Ile Asn Leu Pro Arg Ser Met Asp Phe Glu Glu 200 205 Ala Glu Arg Ser Glu Pro Thr Gln Ala Leu Glu Leu Thr Glu Asp Asp 215 220 Ile Lys Glu Asp Gly Ile Val Pro Leu Arg Tyr Val Lys Phe Gln Asn 230 235 Val Asn Ser Val Thr Ile Phe Val Gln Ser Asn Gln Gly Glu Glu 245 250 Thr Thr Arg Ile Ser Tyr Phe Thr Phe Ile Gly Thr Pro Val Gln Ala 265 260 270 Thr Asn Met Asn Asp Phe Lys Arg Val Val Gly Lys Lys Gly Glu Ser 280 285

<210> 192 <211> 335 <212> PRT

<213> Homo sapien

Met Glu Ala Gly Ala Ala Glu Ala Ala Val Ala Val Glu Glu Val 10 Gly Ser Ala Gly Gln Phe Glu Glu Leu Leu Arg Leu Lys Ala Lys Ser 20. 25 Leu Leu Val Val His Phe Trp Ala Pro Trp Ala Pro Gln Cys Ala Gln 40 Met Asn Glu Val Met Ala Glu Leu Ala Lys Glu Leu Pro Gln Val Ser 55 Phe Val Lys Leu Glu Ala Glu Gly Val Pro Glu Val Ser Glu Lys Tyr 70 75 Glu Ile Ser Ser Val Pro Thr Phe Leu Phe Phe Lys Asn Ser Gln Lys 85 90 Ile Asp Arg Leu Asp Gly Ala His Ala Pro Glu Leu Thr Lys Lys Val 105 Gln Arg His Ala Ser Ser Gly Ser Phe Leu Pro Ser Ala Asn Glu His 120 115 125 Leu Lys Glu Asp Leu Asn Leu Arg Leu Lys Lys Leu Thr His Ala Ala 130 135 140 Pro Cys Met Leu Phe Met Lys Gly Thr Pro Gln Glu Pro Arg Cys Gly 155 Phe Ser Lys Gln Met Val Glu Ile Leu His Lys His Asn Ile Gln Phe 165 170 Ser Ser Phe Asp Ile Phe Ser Asp Glu Glu Val Arg Gln Gly Leu Lys 180 185 190 Ala Tyr Ser Ser Trp Pro Thr Tyr Pro Gln Leu Tyr Val Ser Gly Glu 200

```
Leu Ile Gly Gly Leu Asp Ile Ile Lys Glu Leu Glu Ala Ser Glu Glu
                        215
Leu Asp Thr Ile Cys Pro Lys Ala Pro Lys Leu Glu Glu Arg Leu Lys
                                        235
225
                    230
Val Leu Thr Asn Lys Ala Ser Val Met Leu Phe Met Lys Gly Asn Lys
                245
                                    250
Gln Glu Ala Lys Cys Gly Phe Ser Lys Gln Ile Leu Glu Ile Leu Asn
            260
                                265
Ser Thr Gly Val Glu Tyr Glu Thr Phe Asp Ile Leu Glu Asp Glu Glu
        275
                            280
                                                285
Val Arg Gln Gly Leu Lys Ala Tyr Ser Asn Trp Pro Thr Tyr Pro Gln
                        295
Leu Tyr Val Lys Gly Glu Leu Val Gly Gly Leu Asp Ile Val Lys Glu
                    310
                                       315
Leu Lys Glu Asn Gly Glu Leu Leu Pro Ile Leu Arg Gly Glu Asn
                325
                                    330
```

<210> 193

<211> 131

<212> PRT

<213> Phalaris coerulescens

<400> 193

Met Gly Gly Cys Val Gly Lys Asp Arg Gly Ile Val Glu Asp Lys Leu Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp 20 25 Asp Gln Lys Ile Ala Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala 35 40 45 Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val 55 Tyr Ala Glu Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile Asp Val Asp Asp Leu Val Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala 85 90 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Asp Lys Leu 100 105 110 Val Gly Ala Asn Lys Pro Glu Leu Glu Lys Lys Val Gln Ala Leu Gly 115 120 Asp Gly Ser

130

<210> 194

<211> 144

<212> PRT

<213> Trypanosoma brucei brucei

<400> 194

Met Ser Gly Leu Ala Lys Tyr Leu Pro Gly Ala Thr Asn Leu Leu Ser 10 Lys Ser Gly Glu Val Ser Leu Gly Ser Leu Val Gly Lys Thr Val Phe 20 Leu Tyr Phe Ser Ala Ser Trp Cys Pro Pro Cys Arg Gly Phe Thr Pro Val Leu Ala Glu Phe Tyr Glu Lys Ris His Val Ala Lys Asn Phe Glu 55 60 Val Val Leu Ile Ser Trp Asp Glu Asn Glu Ser Asp Phe His Asp Tyr 70 75 Tyr Gly Lys Met Pro Trp Leu Ala Leu Pro Phe Asp Gln Arg Ser Thr Val Ser Glu Leu Gly Lys Thr Phe Gly Val Glu Ser Ile Pro Thr Leu 105 Ile Thr Ile Asn Ala Asp Thr Gly Ala Ile Ile Gly Thr Gln Ala Arg 120 125 Thr Arg Val Ile Glu Asp Pro Asp Gly Ala Asn Phe Pro Trp Pro Asn

130 135 140

<210> 195 <211> 333 <212> PRT <213> Arabidopsis thaliana

<400> 195 Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser 10 Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly 40 Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro 55 Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser 75 Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp 90 Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu 100 105 Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser 120 Phe Val Gly Ser Gly Glu Ala Ser Gly Gly Phe Trp Asn Arg Gly Ile 135 140 Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys 150 155 Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn 170 Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg Arg Asp 180 1.85 Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro 200 195 205 Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp 210 215 220 Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr 230 235 Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly 245 250 His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser 260 265 Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro 275 280 285 Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala 295 300 Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His 310 315 Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp

<210> 196 <211> 383 <212> PRT <213> Arabidopsis thaliana

```
Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ser Arg Ala
                    70
Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala
                                   90
               85
Pro Gly Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly
                               105
           100
Phe Pro Glu Gly Ile Leu Gly Ile Asp Ile Val Glu Lys Phe Arg Lys
                           120
                                               125
Gln Ser Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Asn Lys
                       135
Val Asp Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Arg Thr
                                       155
                   150
Val Leu Ala Asp Ser Val Ile Ile Ser Thr Gly Ala Val Ala Lys Arg
               165
                                   170
Leu Ser Phe Thr Gly Ser Gly Glu Gly Asn Gly Gly Phe Trp Asn Arg
                               185
                                                   190
          180
Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg
                           200
       195
Asn Lys Pro Leu Val Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu
                       215
                                           220
Ala Asn Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg
                   230
                                       235
Arg Asp Thr Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser
                                   250
               245
Asn Pro Lys Ile Glu Val Ile Trp Asn Ser Ala Val Val Glu Ala Tyr
                               265
                                                   270
           260
Gly Asp Glu Asn Gly Arg Val Leu Gly Gly Leu Lys Val Lys Asn Val
       275
                           280
                                               285
Val Thr Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala
                                           300
                       295
Ile Gly His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gln Leu Glu Leu
                                       315
                   310
Asp Glu Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Lys Thr Ser
               325
                                   330
                                                       335
Val Val Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg
                               345
                                                   350
Gln Ala Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala
                           360
Glu His Tyr Leu Gln Glu Ile Gly Ser Gln Glu Gly Lys Ser Asp
```

<400> 197 Met Ala Val Ser Leu Met Gln Gln Pro Asp Lys Val Tyr Asp Val Ile 10 Ile Ile Gly Ala Gly Pro Ala Gly Thr Thr Ala Ala Ile Tyr Thr Ala 20 25 Arg Ala Gly Trp Lys Thr Leu Val Leu Tyr Arg Ala Glu Ala Asp Gly 40 35 Ala Leu Gly Val Thr Gln Lys Ile Glu Asn Tyr Pro Gly Val Pro Gly 55 60 Pro Leu Ser Gly Tyr Glu Leu Leu Lys Ile Met Arg Glu Gln Ala Lys 70 Ser Phe Gly Ala Glu Phe Val Arg Gly Lys Val Ile Ala Thr Asp Leu 85 90 Asn Ser Asp Pro Lys Lys Val Tyr Thr Ile Asp Gly Arg Glu Phe Arg 105 110 100 Gly Lys Thr Ile Ile Val Ala Ser Gly Ala Met Glu Arg Ala Asn Lys 120 125 Phe Lys Gly Glu Glu Glu Phe Leu Gly Arg Gly Val Ser Tyr Cys Gly 135 Val Cys Asp Ala Ala Phe Phe Lys Asp Gln Pro Val Ala Val Ile Gly

<sup>&</sup>lt;210> 197

<sup>&</sup>lt;211> 323

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Aquifex aeolicus

```
145
                   150
                                       155
Asp Asp Tyr Ala Ile Glu Glu Ala Glu Phe Ile Ala Arg Phe Ala
               165
                                   170
Asn Lys Val Phe Phe Val Val Pro Gly Ser Lys Ile Lys Ala Pro Pro
           180
                               185
Glu Val Ile Glu His Phe Glu Lys Leu Pro Asn Val Glu Ile Leu Leu
                           200
                                               205
Arg His Arg Pro Ile Glu Ile Val Gly Asp Gln Val Val Lys Gly Ile
                       215
                                           220
Lys Leu Lys Asp Leu Glu Lys Lys Glu Glu Lys Leu Leu Glu Val Asn
                                       235
                   230
Gly Val Phe Ile Phe Leu Gly Gly Thr Lys Pro Ser Val Asp Phe Leu
                                   250
               245
Met Gly Gln Val Glu Met Thr Glu Gly Asp Cys Ile Val Val Asn Glu
           260
                               265
Glu Met Met Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Leu
                           280
Cys Asn Glu Val Lys Gln Ala Val Val Ala Ala Met Gly Cys Lys
                       295
                                           300
Ala Ala Leu Ala Val Asp Lys Phe Leu Ser Gly Lys Lys Lys Ile Val
                   310
Pro Gln Trp
```

<210> 198 <211> 315 <212> PRT <213> Bacillus subtilis

<400> 198 Ser Glu Glu Lys Ile Tyr Asp Val Ile Ile Gly Ala Gly Pro Ala Gly Met Thr Ala Ala Val Tyr Thr Ser Arg Ala Asn Leu Ser Thr Leu Met Ile Glu Arg Gly Ile Pro Gly Gly Gln Met Ala Asn Thr Glu Asp Val Glu Asn Tyr Pro Gly Phe Glu Ser Ile Leu Gly Pro Glu Leu Ser Asn Lys Met Phe Glu His Ala Lys Lys Phe Gly Ala Glu Tyr Ala Tyr 70 75 Gly Asp Ile Lys Glu Val Ile Asp Gly Lys Glu Tyr Lys Val Val Lys 90 85 Ala Gly Ser Lys Glu Tyr Lys Ala Arg Ala Val Ile Ile Ala Ala Gly 105 Ala Glu Tyr Lys Lys Ile Gly Val Pro Gly Glu Lys Glu Leu Gly Gly 120 Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Lys Gly 135 140 Lys Glu Leu Val Val Val Gly Gly Asp Ser Ala Val Glu Gly 145 150 155 Val Tyr Leu Thr Arg Phe Ala Ser Lys Val Thr Ile Val His Arg Arg 165 170 Asp Lys Leu Arg Ala Gln Ser Ile Leu Gln Ala Arg Ala Phe Asp Asn 180 185 Glu Lys Val Asp Phe Leu Trp Asn Lys Thr Val Lys Glu Ile His Glu 195 205 200 Glu Asn Gly Lys Val Gly Asn Val Thr Leu Val Asp Thr Val Thr Gly 215 Glu Glu Ser Glu Phe Lys Thr Asp Gly Val Phe Ile Tyr Ile Gly Met 230 235 Leu Pro Leu Ser Lys Pro Phe Glu Asn Leu Gly Ile Thr Asn Glu Glu 245 250 Gly Tyr Ile Glu Thr Asn Asp Arg Met Glu Thr Lys Val Glu Gly Ile 265 270 Phe Ala Ala Gly Asp Ile Arg Glu Lys Ser Leu Arg Gln Ile Val Thr 280

Ala Thr Gly Asp Gly Ser Ile Ala Ala Gln Ser Val Gln His Tyr Val 295 Glu Glu Leu Gln Glu Thr Leu Lys Thr Leu Lys 310 <210> 199 <211> 326 <212> PRT <213> Borrelia burgdorferi <400> 199 Met Leu Glu Phe Glu Thr Ile Asp Ile Asn Leu Thr Lys Lys Lys Asn 10 Leu Ser Gln Lys Glu Val Asp Phe Ile Glu Asp Val Ile Ile Val Gly Ser Gly Pro Ala Gly Leu Thr Ala Gly Ile Tyr Ser Val Met Ser Asn 35 40 45 Tyr Lys Ala Ala Ile Leu Glu Gly Pro Glu Pro Gly Gly Gln Leu Thr 50 55 60 Thr Thr Thr Glu Val Tyr Asn Tyr Pro Gly Phe Lys Asn Gly Ile Ser 70 75 Gly Arg Asn Leu Met Leu Asn Met Arg Glu Gln Val Val Asn Leu Gly 90 85 Ala Lys Thr Phe Pro Glu Thr Val Phe Ser Ile Lys Arg Lys Gly Asn 110 100 105 Ile Phe Tyr Leu Tyr Thr Glu Asn Tyr Ile Tyr Lys Ser Lys Ala Val 115 120 Ile Ile Ala Val Gly Ser Lys Pro Lys Lys Leu Glu Thr Leu Lys Asn 135 140 Ser Gly Leu Phe Trp Asn Lys Gly Ile Ser Val Cys Ala Ile Cys Asp 155 150 Gly His Leu Phe Lys Gly Lys Arg Val Ala Val Ile Gly Gly Gly Asn 165 170 175 Thr Ala Leu Ser Glu Ser Ile Tyr Leu Ser Lys Leu Val Asp Lys Val 180 185 190 Tyr Leu Ile Val Arg Lys Asn Asn Leu Arg Ala Ile Ala Met Leu Arg 200 195 Asp Ser Val Ala Lys Leu Pro Asn Ile Glu Ile Leu Tyr Asn Ser Glu 215 220 Ala Ile Glu Val Asp Gly Lys Ser Ser Val Ser Ser Val Lys Ile Phe 230 235 Asn Lys Lys Asp Asn Val Val Tyr Glu Leu Glu Val Ser Ala Val Phe 250 245 Met Ala Val Gly Tyr Lys Pro Asn Thr Glu Phe Leu Lys Gly Phe Leu 270 260 265 Asp Leu Asp Glu Glu Gly Phe Ile Val Thr Lys Asp Val Val Lys Thr 275 280 Ser Val Asp Gly Val Phe Ser Cys Gly Asp Val Ser Asn Lys Leu Tyr 295 300 Ala Gln Ala Ile Thr Ala Ala Ala Glu Gly Phe Ile Ala Ser Val Glu 310 Leu Gly Asn Phe Leu Lys 325 <210> 200 <211> 319 <212> PRT <213> Buchnera aphidicola <400> 200 Met Asp Lys Val Lys His Ser Lys Ile Ile Ile Leu Gly Ser Gly Pro 10 15

Ala Gly Tyr Thr Ala Ala Ile Tyr Ala Ala Arg Ala Asn Leu Asp Pro
20 25 30
Phe Leu Ile Thr Gly Thr Asn Lys Gly Gly Gln Leu Met Asn Thr Asn

```
40
Glu Ile Glu Asn Trp Pro Gly Asp Tyr Asn Lys Ile Ser Gly Ser Glu
                    55
Leu Met Asn Arg Met Tyr Lys His Ala Ile Glu Leu Lys Thr Lys Val
                   70
Ile Cys Asp Thr Val Ile Ser Val Asn Phe Lys Lys Asn Pro Phe Phe
Leu Ile Gly Glu Asn Asn Lys Tyr Thr Ala Asp Ser Val Ile Ile Ala
                               105
Thr Gly Ala Asn Pro Arg Tyr Leu Gly Leu Gln Ser Glu Ser Leu Phe
                           120
                                               125
Lys Gly Lys Gly Val Ser Thr Cys Ala Val Cys Asp Gly Phe Phe Tyr
                       135
Lys Asn Lys Glu Val Ala Val Val Gly Gly Asn Thr Ala Ile Glu
                   150
                                       155
Glu Thr Leu Tyr Leu Ser Asn Phe Val Lys Lys Val His Leu Ile His
               165
                                   170
Arg Gly Ile Asn Phe Arg Ala Glu Lys Ile Leu Leu Asp Arg Leu Glu
                                185
Lys Lys Ile Lys Ser Gln Lys Ile Ile Ile Tyr Leu Asn Ser Ile Val
                           200
Lys Asn Ile Leu Gly Asn Ser Ser Gly Val Thr Ala Leu Leu Ile Glu
                                           220
                       215
Gln Lys Asn Ser Lys Glu Lys Thr Glu Ser Lys Ile Gln Val Ser Gly
                  . 230
                                       235
Leu Phe Val Ala Ile Gly Tyr Thr Pro Asn Thr Asn Ile Phe Val Asn
                                   250
Lys Leu Lys Met Lys Asp Gly Tyr Ile Gln Val Thr Arg Gln Glu His
           260
                               265
Gly Asn Tyr Thr Gln Thr Ser Ile Pro Gly Ile Phe Ala Ala Gly Asp
        275
                           280
Val Ile Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ser Ala Ser Gly
                       295
Cys Met Ala Ala Leu Asp Ser Glu Arg Tyr Ile Asn Ser Leu Val
```

<210> 201 <211> 319 <212> PRT

<213> Buchnera aphidicola

<400> 201 Met Glu Leu Lys Asn His Lys Lys Ile Ile Ile Leu Gly Ser Gly Pro 10 Ala Gly Tyr Thr Ala Ala Ile Tyr Ser Ser Arg Ala Asn Leu Asn Pro 20 Leu Leu Ile Thr Gly Ile Asn Lys Gly Gly Gln Leu Met Asn Thr Asn Glu Ile Glu Asn Trp Pro Gly Asp Phe Lys Lys Ile Thr Gly Pro Glu 55 Leu Met Asn Arg Met His Glu His Ser Leu Lys Phe Lys Thr Glu Ile 75 Val Tyr Asp Asn Ile Ile Ser Val Glu Phe Lys Lys Lys Pro Phe Phe 85 90 Leu Leu Gly Glu Tyr Asn Lys Tyr Thr Cys Asp Ala Val Ile Ile Ala 105 Thr Gly Ala Asn Pro Arg Tyr Leu Gly Leu Ser Ser Glu Asn Lys Phe 120 Lys Gly Lys Gly Ile Ser Thr Cys Ala Val Cys Asp Gly Phe Phe Tyr 135 140 Lys Asn Lys Glu Ile Ala Val Val Gly Gly Asn Thr Ala Ile Glu 150 155 Glu Thr Leu Tyr Leu Ser Asn Phe Val Lys Lys Ile Tyr Leu Ile His 170 Arg Arg Asn Asn Phe Lys Ala Glu Lys Ile Leu Ile Asp Arg Leu Leu 185

Lys Ile Val Lys Thr Lys Lys Val Ile Leu His Leu Asn Ser Thr Ile 200 Glu Asp Ile Leu Gly Asn Asn Lys Gly Val Thr His Leu Leu Ile Lys 215 220 Asn Lys Asn Leu Lys Glu Lys Lys Lys Leu Lys Ile Ala Val Ser Gly 230 235 Leu Phe Val Ala Ile Gly Tyr Ile Pro Asn Thr Asp Ile Phe Thr Asp 245 250 Gln Leu Lys Met Lys Asp Gly Tyr Ile Lys Ile Lys Lys Gly Thr His 265 270 Gly Asn Tyr Thr Gln Thr Asn Ile Pro Gly Val Phe Ala Ala Gly Asp 275 280 285 Val Ile Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ser Ala Ser Gly 295 290 300 Cys Met Ala Ala Leu Asp Ser Glu Arg Tyr Leu Asn Ser Leu Ser

<210> 202

<211> 312

<212> PRT

<213> Chlamydia muridarum

<400> 202 Met Thr His Val Lys Leu Ala Ile Ile Gly Ser Gly Pro Ala Gly Tyr 10 Thr Ala Ala Ile Tyr Ala Ser Arg Ala Leu Leu Thr Pro Ile Leu Phe 25 Glu Gly Phe Phe Ser Gly Ile Ala Gly Gly Gln Leu Met Thr Thr 35 40 Glu Val Glu Asn Phe Pro Gly Phe Pro Gln Gly Val Leu Gly His Gln 55 Leu Met Glu Asn Met Lys Met Gln Ala Gln Arg Phe Gly Thr Gln Val 70 75 Ile Ala Lys Asp Ile Thr Ser Val Asp Phe Ser Val Arg Pro Phe Val 85 90 Leu Lys Ser Gly Glu Asp Thr Phe Thr Cys Asp Ala Cys Ile Ile Ala 105 Thr Gly Ala Ser Ala Lys Arg Leu Ser Ile Pro Gly Ala Gly Asp Asn 120 125 Glu Phe Trp Gln Lys Gly Val Thr Ala Cys Ala Val Cys Asp Gly Ala 135 140 Ser Pro Ile Phe Arg Asp Arg Asp Leu Phe Val Ile Gly Gly Asp 150 155 Ser Ala Leu Glu Glu Ala Met Phe Leu Thr Arg Tyr Gly Lys Arg Val 170 175 Phe Val Val His Arg Arg Asp Thr Leu Arg Ala Ser Lys Ala Met Val 180 185 190 Asn Lys Ala Gln Ala Asn Glu Lys Ile Val Phe Leu Trp Asn Ser Glu 200 195 . 205 Val Val Lys Ile Leu Gly Asp Ser Leu Val Arg Ser Ile Asp Ile Phe 215 220 Asn Asn Val Glu Lys Thr Thr Val Thr Met Glu Ala Ala Gly Val Phe 230 235 Phe Ala Ile Gly His Gln Pro Asn Thr Ala Phe Leu Gly Gly Gln Leu 245 250 · 255 Ser Leu Asp Glu Asn Gly Tyr Ile Ile Thr Glu Lys Gly Ser Ser Arg 270 260 265 Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Tyr 275 280 Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly Cys Met Ala Ala Leu 295 Asp Ala Glu Arg Phe Leu Glu Lys 310

<210> 203

<211> 311 <212> PRT <213> Chlamydia pneumoniae <400> 203 Met Ile His Ser Arg Leu Ile Ile Ile Gly Ser Gly Pro Ser Gly Tyr 10 Thr Ala Ala Ile Tyr Ala Ser Arg Ala Leu Leu His Pro Leu Leu Phe 25 Glu Gly Phe Phe Ser Gly Ile Ser Gly Gly Gln Leu Met Thr Thr Glu Val Glu Asn Phe Pro Gly Phe Pro Glu Gly Ile Leu Gly Pro Lys 55 Leu Met Asn Asn Met Lys Glu Gln Ala Val Arg Phe Gly Thr Lys Thr 70 Leu Ala Gln Asp Ile Ile Ser Val Asp Phe Ser Val Arg Pro Phe Ile 90 Leu Lys Ser Lys Glu Glu Thr Tyr Ser Cys Asp Ala Cys Ile Ile Ala 100 105 Thr Gly Ala Ser Ala Lys Arg Leu Glu Ile Pro Gly Ala Gly Asn Asp 120 125 Glu Phe Trp Gln Lys Gly Val Thr Ala Cys Ala Val Cys Asp Gly Ala 135 140 Ser Pro Ile Phe Lys Asn Lys Asp Leu Tyr Val Ile Gly Gly Asp 150 155 Ser Ala Leu Glu Glu Ala Leu Tyr Leu Thr Arg Tyr Gly Ser His Val 170 165 175 Tyr Val Val His Arg Arg Asp Lys Leu Arg Ala Ser Lys Ala Met Glu √ 185 Ala Arg Ala Gln Asn Asn Glu Lys Ile Thr Phe Leu Trp Asn Ser Glu 205 200 Ile Val Lys Ile Ser Gly Asp Ser Ile Val Arg Ser Val Asp Ile Lys 215 220 Asn Val Gln Thr Gln Glu Ile Thr Thr Arg Glu Ala Ala Gly Val Phe 235 230 Phe Ala Ile Gly His Lys Pro Asn Thr Asp Phe Leu Gly Gly Gln Leu 245 250 Thr Leu Asp Glu Ser Gly Tyr Ile Val Thr Glu Lys Gly Thr Ser Lys 265 Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Tyr 280 285 Tyr Arg Gln Ala Val Thr Ser Ala Gly Ser Gly Cys Ile Ala Ala Leu 300 295 Asp Ala Glu Arg Phe Leu Gly <210> 204 <211> 312 <212> PRT <213> Chlamydia trachomatis <400> 204 Met Thr His Ala Lys Leu Val Ile Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Ile Tyr Ala Ser Arg Ala Leu Leu Thr Pro Val' Leu Phe 20 25 Glu Gly Phe Phe Ser Gly Ile Ala Gly Gly Gln Leu Met Thr Thr Glu Val Glu Asn Phe Pro Gly Phe Pro Glu Gly Val Leu Gly His Gln 55 Leu Met Asp Leu Met Lys Thr Gln Ala Gln Arg Phe Gly Thr Gln Val 70 75 Leu Ser Lys Asp Ile Thr Ala Val Asp Phe Ser Val Arg Pro Phe Val 85 90

Leu Lys Ser Gly Lys Glu Thr Phe Thr Cys Asp Ala Cys Ile Ile Ala

```
Thr Gly Ala Ser Ala Lys Arg Leu Ser Ile Pro Gly Ala Gly Asp Asn
                            120
Glu Phe Trp Gln Lys Gly Val Thr Ala Cys Ala Val Cys Asp Gly Ala
   130
                       135
                                           140
Ser Pro Ile Phe Arg Asp Lys Asp Leu Phe Val Val Gly Gly Asp
                   150
                                       155
Ser Ala Leu Glu Glu Ala Met Phe Leu Thr Arg Tyr Gly Lys Arg Val
                                                        175
                                   170
Phe Val Val His Arg Arg Asp Thr Leu Arg Ala Ser Lys Val Met Val
                               185
Asn Lys Ala Gln Ala Asn Glu Lys Ile Phe Phe Leu Trp Asn Ser Glu
                                               205
                           200
Ile Val Lys Ile Ser Gly Asp Thr Leu Val Arg Ser Ile Asp Ile Tyr
                        215
Asn Asn Val Asp Glu Thr Thr Thr Thr Met Glu Ala Ala Gly Val Phe
                   230
                                       235
Phe Ala Ile Gly His Gln Pro Asn Thr Ala Phe Leu Gly Gly Gln Val
               245
                                   250
Ala Leu Asp Glu Asn Gly Tyr Ile Ile Thr Glu Lys Gly Ser Ser Arg
                               265
Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Tyr
       275
                           280
Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly Cys Met Ala Ala Leu
                       295
Asp Ala Glu Arg Phe Leu Glu Asn
                   310
```

<210> 205

<211> 315

<212> PRT

<213> Clostridium litorale

<400> 205 Met Glu Asn Val Tyr Asp Ile Ala Ile Ile Gly Ser Gly Pro Ala Gly Leu Ala Ala Ala Leu Tyr Gly Ala Arg Ala Lys Met Lys Thr Leu Leu 20 Leu Glu Gly Met Lys Val Gly Gly Gln Ile Val Ile Thr His Glu Val 40 Ala Asn Tyr Pro Gly Ser Val Pro Glu Ala Thr Gly Pro Ser Leu Ile 55 Gly Arg Met Glu Glu Gln Val Glu Glu Phe Gly Ala Glu Arg Val Met 75 Asp Asn Ile Val Asp Val Asp Phe Thr Asp Lys Ile Lys Val Leu Lys 90 85 Gly Ala Lys Gly Glu Tyr Lys Ala Lys Ala Val Ile Val Ala Thr Gly 100 105 110 Ala Ser Pro Lys Leu Ala Gly Cys Pro Gly Glu Lys Glu Leu Thr Gly 115 120 Lys Gly Val Ser Tyr Cys Ala Thr Cys Asp Ala Asp Phe Phe Glu Asp 135 140 Met Glu Val Phe Val Ile Gly Gly Asp Thr Ala Val Glu Glu Ala 150 155 Met Phe Leu Thr Lys Phe Ala Arg Lys Val Thr Ile Val His Arg Arg 165 170 Ala Glu Leu Arg Ala Ala Lys Ser Ile Gln Glu Lys Ala Phe Lys Asn 180 185 190 Glu Lys Leu Asn Phe Met Trp Asn Thr Val Ile Glu Glu Ile Lys Gly 200 195 205 Asp Gly Ile Val Glu Ser Ala Val Phe Lys Asn Arg Glu Thr Gly Glu 215 220 Val Thr Glu Phe Val Ala Pro Glu Glu Asp Gly Thr Phe Gly Ile Phe 235 Val Phe Ile Gly Tyr Asp Pro Lys Ser Ala Leu Val Glu Gly Lys Leu 245 250 Glu Leu Asp Glu Thr Gly Tyr Ile Pro Thr Asp Asp Asn Met Lys Thr

```
260
                               265
Asn Val Glu Gly Val Phe Ala Ala Gly Asp Ile Arg Val Lys Ser Leu
                         280
Arg Gln Val Val Thr Ala Thr Ala Asp Gly Ala Ile Ala Ala Val Gln
                        295
Ala Glu Lys Tyr Ile Glu Glu Leu Phe Ala Glu
<210> 206
<211> 321
<212> PRT
<213> Coxiella burnetii
<400> 206
Met Asn Lys Pro Gln His His Ser Leu Ile Ile Leu Gly Ser Gly Pro
                5
                                   10
Ala Gly Tyr Thr Asp Ala Ile Tyr Val Ala Arg Ala Asn Leu Lys Pro
           20
                               25
Ile Met Ile Thr Gly Met Glu Gln Gly Gly Gln Leu Met Thr Thr Thr
                            40
Asp Val Ala Asn Trp Pro Gly Glu Ala Pro Gly Leu Gln Gly Pro Lys
                       55
Leu Leu Glu Arg Met Gln Lys His Ala Gly Gly Ala Leu Asn Thr Gln
                   70
                                       75
Phe Ile Phe Asp His Ile Asn Lys Pro Asp Leu Asn Pro Arg Pro Phe
               85
                                   90
Leu Leu Gln Gly Asp Asn Ala Thr Tyr Ser Cys Asp Ala Leu Ile Ile
                               105
Ala Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Lys Pro
       115
                           120
                                               125
Tyr Met Gly Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe
                       135
                                           140
Tyr Arg Ala Lys Lys Val Ala Val Val Gly Gly Asn Thr Ser Val
                  150
                                       155
Glu Glu Ala Leu Tyr Leu Ser His Ile Ala Ser His Val Thr Leu Ile
             165
                                   170
                                                       175
His Arg Arg Asp Lys Leu Arg Ala Glu Lys Met Leu Ser Ala Gln Leu
           180
                               185
                                                190
Ile Lys Lys Val Glu Glu Gly Lys Val Ala Ile Val Trp Ser His Val
       195
                           200
                                               205
Ile Glu Glu Val Leu Gly Asp Asp Gln Gly Val Thr Gly Val His Leu
                       215
                                           220
Lys His Val Lys Glu Glu Lys Thr Gln Asp Leu Thr Ile Asp Gly Leu
                   230
                                       235
Phe Ile Ala Ile Gly His Asp Pro Asn Thr Lys Ile Phe Lys Glu Gln
               245
                                   250
Leu Glu Met Asp Glu Ala Gly Tyr Leu Arg Ala Lys Ser Gly Leu Gln
                                                  270
                               265
Gly Asn Ala Thr Ala Thr Asn Ile Pro Gly Val Phe Pro Ala Val Val
                           280
Val Arg Gly Gln Leu Tyr Arg Gln Thr Ile Ala Ala Gly Met Gly
                      295
                                          300
Cys Met Pro Ala Leu Asp Ala Glu Arg Tyr Leu Asp Ser Leu Asn Gln
305
                   310
Ala
<210> 207
<211> 320
<212> PRT
<213> Escherichia coli
<400> 207
Gly Thr Thr Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro Ala
```

Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro Val Leu Ile Thr Gly Met Glu Lys Gly Gly Gln Leu Thr Thr Thr Glu 35 40 Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu Leu 55 Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile Ile Phe Asp His Ile Asn Lys Val Asp Leu Gln Asn Arg Pro Phe Arg Leu 90 Asn Gly Asp Asn Gly Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ala Thr 100 105 110 Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe Lys 120 125 Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr Arg 135 140 Asn Gln Lys Val Ala Val Ile Gly Gly Gly Asn Thr Ala Val Glu Glu 150 155 Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Ile His Arg 165 170 Arg Asp Gly Phe Arg Ala Glu Lys Ile Leu Ile Lys Arg Leu Met Asp 185 190 Lys Val Glu Asn Gly Asn Ile Ile Leu His Thr Asn Arg Thr Leu Glu 200 205 195 Glu Val Thr Gly Asp Gln Met Gly Val Thr Gly Val Arg Leu Arg Asp 215 220 Thr Gln Asn Ser Asp Asn Ile Glu Ser Leu Asp Val Ala Gly Leu Phe 235 Val Ala Ile Gly His Ser Pro Asn Thr Ala Ile Phe Glu Gly Gln Leu 245 250 Glu Leu Glu Asn Gly Tyr Ile Lys Val Gln Ser Gly Ile His Gly Asn 260 265 270 Ala Thr Gln Thr Ser Ile Pro Gly Val Phe Ala Ala Gly Asp Val Met 275 280 285 Asp His Ile Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys Met 295 300 Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Gly Leu Ala Asp Ala Lys

<400> 208 Met Glu Asn Val Tyr Asp Leu Ala Ile Ile Gly Ser Gly Pro Ala Gly Leu Ala Ala Leu Tyr Gly Ala Arg Ala Lys Met Lys Thr Ile Met Ile Glu Gly Gln Lys Val Gly Gly Gln Ile Val Ile Thr His Glu Val Ala Asn Tyr Pro Gly Ser Val Arg Glu Ala Thr Gly Pro Ser Leu Ile 55 60 Glu Arg Met Glu Glu Gln Ala Asn Glu Phe Gly Ala Glu Lys Val Met 70 75 Asp Lys Ile Val Asp Val Asp Leu Asp Gly Lys Ile Lys Val Ile Lys 90 Gly Glu Lys Ala Glu Tyr Lys Ala Lys Ser Val Ile Leu Ala Thr Gly 105 Ala Ala Pro Arg Leu Ala Gly Cys Pro Gly Glu Gln Glu Leu Thr Gly 120 115 125 Lys Gly Val Ser Tyr Cys Ala Thr Cys Asp Ala Asp Phe Phe Glu Asp 130 140 135 Met Glu Val Phe Val Val Gly Gly Gly Asp Thr Ala Val Glu Glu Ala 150 155 Met Tyr Leu Ala Lys Phe Ala Arg Lys Val Thr Ile Val His Arg Arg

<sup>&</sup>lt;210> 208 <211> 315

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Eubacterium acidaminophilum

```
165
                                    170
Asp Glu Leu Arg Ala Ala Lys Ser Ile Gln Glu Lys Ala Phe Lys Asn
           180
                          185
Pro Lys Leu Asp Phe Met Trp Asn Ser Ala Ile Glu Glu Ile Lys Gly
                          200
Asp Gly Ile Val Glu Ser Ala Val Phe Lys Asn Leu Val Thr Gly Glu
                        215
Thr Thr Glu Tyr Phe Ala Asn Glu Glu Asp Gly Thr Phe Gly Ile Phe
                    230
                                        235
Val Phe Ile Gly Tyr Ile Pro Lys Ser Asp Val Phe Lys Gly Lys Ile
                245
                                    250
Thr Leu Asp Asp Ala Gly Tyr Ile Ile Thr Asp Asp Asn Met Lys Thr
                                265
Asn Val Glu Gly Val Phe Ala Ala Gly Asp Ile Arg Val Lys Ser Leu
                           280
                                               285
Arg Gln Val Val Thr Ala Cys Ala Asp Gly Ala Ile Ala Ala Thr Gln
                       295
Ala Glu Lys Tyr Val Glu Ala Asn Phe Glu Glu
<210> 209
<211> 318
<212> PRT
<213> Haemophilus influenzae
<400> 209
Met Ser Asp Ile Lys His Ala Lys Leu Leu Ile Leu Gly Ser Gly Pro
                                    10
Ala Gly Tyr Thr Ala Ala Ile Tyr Ala Ala Arg Ala Asn Leu Lys Pro
            20
                                25
Val Leu Val Thr Gly Leu Gln Gln Gly Gly Gln Leu Thr Thr Asp
Glu Ile Glu Asn Trp Pro Gly Asp Phe Glu Met Thr Thr Gly Ser Gly
                        55
                                            60
Leu Met Gln Arg Met Leu Gln His Ala Glu Lys Phe Glu Thr Glu Ile
                   70
                                        75
Val Phe Asp His Ile Asn Arg Val Asp Leu Ser Ser Arg Pro Phe Lys
              85
                                    90
Leu Phe Gly Asp Val Gln Asn Phe Thr Cys Asp Ala Leu Ile Ile Ala
            100
                                105
Thr Gly Ala Ser Ala Arg Tyr Ile Gly Leu Pro Ser Glu Glu Asn Tyr
                           120
Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr
                        135
                                           140
Arg Asn Lys Pro Val Gly Val Ile Gly Gly Gly Asn Thr Ala Val Glu
                   150
                                       155
Glu Ala Leu Tyr Leu Ala Asn Ile Ala Ser Thr Val His Leu Ile His
                                   170
Arg Arg Asp Ser Phe Arg Ala Glu Lys Ile Leu Ile Asp Arg Leu Tyr
                                185
                                                   190
Lys Lys Val Glu Glu Gly Lys Ile Val Leu His Thr Asp Arg Thr Leu
                            200
                                               205
Asp Glu Val Leu Gly Asp Asn Met Gly Val Thr Gly Leu Arg Leu Ala
                       215
                                           220
Asn Thr Lys Thr Gly Glu Lys Glu Glu Leu Lys Leu Asp Gly Leu Phe
                    230
                                       235
Val Ala Ile Gly His Ser Pro Asn Thr Glu Ile Phe Gln Gly Gln Leu
               245
                                   250
Glu Leu Asn Asn Gly Tyr Ile Val Val Lys Ser Gly Leu Asp Gly Asn
           260
                               265
                                                   270
Ala Thr Ala Thr Ser Val Glu Gly Val Phe Ala Ala Gly Asp Val Met
                            280
                                               285
Asp His Asn Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys Met
                       295
Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Ala Gln Glu Ala
```

```
<210> 210
<211> 311
<212> PRT
<213> Helicobacter pylori
<400> 210
Met Ile Asp Cys Ala Ile Ile Gly Gly Gly Pro Ala Gly Leu Ser Ala
                                    10
Gly Leu Tyr Ala Thr Arg Gly Gly Val Lys Asn Ala Val Leu Phe Glu
                                25
Lys Gly Met Pro Gly Gly Gln Ile Thr Gly Ser Ser Glu Ile Glu Asn
        35
                            40
Tyr Pro Gly Val Lys Glu Val Val Ser Gly Leu Asp Phe Met Gln Pro
                        55
Trp Gln Glu Gln Cys Phe Arg Phe Gly Leu Lys His Glu Met Thr Ala
                    70
                                        75
Ile Gln Arg Val Ser Lys Lys Gly Ser His Phe Val Ile Leu Ala Glu
                                    90
Asp Gly Lys Thr Phe Glu Ala Lys Ser Val Ile Ile Ala Thr Gly Gly
            100
                                105
Ser Pro Lys Arg Thr Gly Ile Lys Gly Glu Ser Glu Tyr Trp Gly Lys
        115
                            120
                                                125
Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn Lys
                        135
                                            140
Glu Val Ala Val Leu Gly Gly Gly Asp Thr Ala Val Glu Glu Ala Ile
                   150
                                     155
Tyr Leu Ala Asn Ile Cys Lys Lys Val Tyr Leu Ile His Arg Arg Asp
                                                        175
               165
                                    170
Gly Phe Arg Cys Ala Pro Ile Thr Leu Glu His Ala Lys Asn Asn Ser
            180
                                185
                                                    190
Lys Ile Glu Phe Leu Thr Pro Tyr Val Val Glu Glu Ile Lys Gly Asp
                            200
Ala Ser Gly Val Ser Ser Leu Ser Ile Lys Asn Thr Ala Thr Asn Glu
                        215
                                            220
Lys Arg Glu Leu Val Val Pro Gly Leu Phe Ile Phe Val Gly Tyr Asp
                    230
                                        235
Val Asn Asn Ala Val Leu Lys Gln Glu Asp Asn Ser Met Leu Cys Glu
               245
                                   250
                                                        255
Cys Asp Glu Tyr Gly Ser Ile Val Val Asp Phe Ser Met Lys Thr Asn
            260
                                265
Val Gln Gly Leu Phe Ala Ala Gly Asp Ile Arg Ile Phe Ala Pro Lys
        275
                            280
                                                285
Gln Val Val Cys Ala Ala Ser Asp Gly Ala Thr Ala Ala Leu Ser Val
                        295
Ile Ser Tyr Leu Glu His His
<210> 211
<211> 311
<212> PRT
<213> Helicobacter pylori
<400> 211
Met Ile Asp Cys Ala Ile Ile Gly Gly Gly Pro Ala Gly Leu Ser Ala
                                    10
                                                        15
Gly Leu Tyr Ala Thr Arg Gly Gly Val Lys Asn Ala Val Leu Phe Glu
           20
                                25
Lys Gly Met Pro Gly Gly Gln Ile Thr Gly Ser Ser Glu Ile Glu Asn
Tyr Pro Gly Val Lys Glu Val Val Ser Gly Leu Asp Phe Met Gln Pro
Trp Gln Glu Gln Cys Phe Arg Phe Gly Leu Lys His Glu Met Thr Ala
                                        75
```

90

Val Gln Arg Val Ser Lys Lys Asp Ser His Phe Val Ile Leu Ala Glu

Asp Gly Lys Thr Phe Glu Ala Lys Ser Val Ile Ile Ala Thr Gly Gly 105 Ser Pro Lys Arg Thr Gly Ile Lys Gly Glu Ser Glu Tyr Trp Gly Lys 120 Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn Lys 135 140 Glu Val Ala Val Leu Gly Gly Gly Asp Thr Ala Val Glu Glu Ala Ile 150 155 Tyr Leu Ala Asn Ile Cys Lys Lys Val Tyr Leu Ile His Arg Arg Asp 165 170 Gly Phe Arg Cys Ala Pro Ile Thr Leu Glu His Ala Lys Asn Asn Asp 180 185 Lys Ile Glu Phe Leu Thr Pro Tyr Val Val Glu Glu Ile Lys Gly Asp 195 200 Ala Ser Gly Val Ser Ser Leu Ser Ile Lys Asn Thr Ala Thr Asn Glu 215 220 Lys Arg Glu Leu Val Val Pro Gly Phe Phe Ile Phe Val Gly Tyr Asp 230 235 Val Asn Asn Ala Val Leu Lys Gln Glu Asp Asn Ser Met Leu Cys Lys 245 250 Cys Asp Glu Tyr Gly Ser Ile Val Val Asp Phe Ser Met Lys Thr Asn 260 265 270 Val Gln Gly Leu Phe Ala Ala Gly Asp Ile Arg Ile Phe Ala Pro Lys 280 285 Gln Val Val Cys Ala Ala Ser Asp Gly Ala Thr Ala Ala Leu Ser Val 295 Ile Ser Tyr Leu Glu His His

<210> 212

<211> 319

<212> PRT

<213> Listeria monocytogenes

<400> 212

Met Ala Ser Glu Glu Lys Ile Tyr Asp Val Ile Ile Ile Gly Ala Gly 10 Pro Ala Gly Met Thr Ala Ala Leu Tyr Thr Ser Arg Ala Asp Leu Asp 25 Thr Leu Met Ile Glu Arg Gly Val Pro Gly Gly Gln Met Val Asn Thr 40 Ala Glu Val Glu Asn Tyr Pro Gly Phe Asp Ser Ile Leu Gly Pro Asp 55 60 Leu Ser Asp Lys Met Leu Ser Gly Ala Lys Gln Phe Gly Ala Glu Tyr 70 Ala Tyr Gly Asp Ile Lys Glu Val Val Asp Gly Lys Glu Phe Lys Thr 85 90 Val Thr Ala Gly Ser Lys Thr Tyr Lys Ala Arg Ala Ile Ile Ala 100 105 110 Thr Gly Ala Glu His Arg Lys Leu Gly Ala Ala Gly Glu Glu Glu Leu 115 120 125 Ser Gly Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe 135 140 Lys Asn Arg Glu Leu Ile Val Val Gly Gly Gly Asp Ser Ala Val Glu 150 155 Glu Gly Thr Tyr Leu Thr Arg Tyr Ala Asp Lys Val Thr Ile Val His 170 165 Arg Arg Asp Lys Leu Arg Ala Gln Gln Ile Leu Gln Asp Arg Ala Phe 180 185 Lys Asp Glu Lys Val Asp Phe Ile Trp Asn Ser Thr Val Glu Glu Ile 200 205 Val Gly Asp Gly Lys Lys Val Thr Gly Ala Lys Leu Val Ser Thr Val 210 220 215 Asp Gly Ser Glu Ser Ile Met Pro Val Asp Gly Val Phe Ile Tyr Val 235 230 Gly Leu Val Pro Leu Thr Lys Ala Phe Leu Asn Leu Gly Ile Thr Asp

```
250
                245
Asp Glu Gly Tyr Ile Val Thr Asp Glu Glu Met Arg Thr Asn Leu Pro
                                265
            260
Gly Ile Phe Ala Ala Gly Asp Val Arg Ala Lys Ser Leu Arg Gln Ile
                            280
Val Thr Ala Thr Gly Asp Gly Gly Leu Ala Gly Gln Asn Ala Gln Lys
                       295
Tyr Val Glu Glu Leu Lys Glu Ser Leu Glu Ala Glu Ala Ala Lys
                    310
<210> 213
<211> 315
<212> PRT
<213> Mycoplasma genitalium
<400> 213
Met Leu Lys Val Asn Ala Asp Phe Leu Thr Lys Asp Gln Val Ile Tyr
                                    10
Asp Leu Val Ile Val Gly Ala Gly Pro Ala Gly Ile Ala Ser Ala Ile
            20
                                25
Tyr Gly Lys Arg Ala Asn Leu Asn Leu Ala Ile Ile Glu Gly Asn Thr
Pro Gly Gly Lys Ile Val Lys Thr Asn Ile Val Glu Asn Tyr Pro Gly
                        55
Phe Lys Thr Ile Thr Gly Pro Glu Leu Gly Leu Glu Met Tyr Asn His
                    70
                                        75
Leu Leu Ala Phe Glu Pro Val Val Phe Tyr Asn Asn Leu Ile Lys Ile
                                    90
               85
Asp His Leu Asn Asp Thr Phe Ile Leu Tyr Leu Asp Asn Lys Thr Thr
                                105
Val Phe Ser Lys Thr Val Ile Tyr Ala Thr Gly Met Glu Glu Arg Lys
                            120
Leu Gly Ile Glu Lys Glu Asp Tyr Phe Tyr Gly Lys Gly Ile Ser Tyr
                       135
                                           140
Cys Ala Ile Cys Asp Ala Ala Leu Tyr Lys Gly Lys Thr Val Gly Val
                                        155
                    150
Val Gly Gly Gly Asn Ser Ala Ile Gln Glu Ala Ile Tyr Leu Ser Ser
                165
                                   170
Ile Ala Lys Thr Val His Leu Ile His Arg Arg Glu Val Phe Arg Ser
           180
                                185
                                                    190
Asp Ala Leu Leu Val Glu Lys Leu Lys Lys Ile Ser Asn Val Val Phe
                            200
                                                205
His Leu Asn Ala Thr Val Lys Gln Leu Ile Gly Gln Glu Lys Leu Gln
                        215
                                            220
Thr Val Lys Leu Ala Ser Thr Val Asp Lys Ser Glu Ser Glu Ile Ala
                    230
                                        235
Ile Asp Cys Leu Phe Pro Tyr Ile Gly Phe Glu Ser Asn Asn Lys Pro
                                    250
               245
Val Leu Asp Leu Lys Leu Asn Leu Asp Gln Asn Gly Phe Ile Leu Gly
                                265
Asp Glu Asn Met Gln Thr Asn Ile Lys Gly Phe Tyr Val Ala Gly Asp
        275
                            280
Cys Arg Ser Lys Ser Phe Arg Gln Ile Ala Thr Ala Ile Ser Asp Gly
                       295
                                            300
Val Thr Ala Val Leu Lys Val Arg Asp Asp Ile
                    310
<210> 214
<211> 458
<212> PRT
<213> Mycobacterium leprae
Met Asn Thr Thr Pro Ser Ala His Glu Thr Ile His Glu Val Ile Val
                                    10
```

```
Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Ala Ala Arg
Ala Gln Leu Thr Pro Leu Val Phe Glu Gly Thr Ser Phe Gly Gly Ala
        35
                            40
Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly
                        55
                                           60
Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg
Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg
                85
                                    90
Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala
            100
                               105
                                                   110
Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile
        115
                            120
Pro Gly Glu Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr
                  · 135
Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly
                                       155
                    150
Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg
                                    170
Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile
                               185
Met Leu Gly Arg Ala Arg Asn Asn Asp Lys Ile Lys Phe Ile Thr Asn
       195
                           200
                                               205
His Thr Val Val Ala Val Asn Gly Tyr Thr Thr Val Thr Gly Leu Arg
    210
                        215
                                           220
Leu Arg Asn Thr Thr Gly Glu Glu Thr Thr Leu Val Val Thr Gly
                   230
                                      235
Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Ser Leu Val Ser Asp
                                   250
                245
Val Val Asp Ile Asp Pro Asp Gly Tyr Val Leu Val Lys Gly Arg Thr
            260
                               265
                                                   270
Thr Ser Thr Ser Met Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp
                           280
                                               285
Arg Thr Tyr Arg Gln Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala
                        295
                                           300
Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Gly Ser Lys Ala
                   310
                                       315
Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr Thr
                                   330
                325
                                                       335
Asp Trp Ser Thr Ala Met Thr Asp Ala Lys Asn Ala Gly Val Thr Ile
            340
                               345
Glu Val Thr Asp Ala Ser Phe Phe Ala Asp Val Leu Ser Ser Asn Lys
                           360 -
Pro Val Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Lys Met
   370
                       375
                                           380
Val Ala Pro Val Leu Glu Glu Ile Ala Ser Glu Gln Arg Asn Gln Leu
                    390
                                       395
Thr Val Ala Lys Leu Asp Val Asp Thr Asn Pro Glu Met Ala Arg Glu
               405
                                  410
Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gln
                               425
                                                   430
Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg
                           440
Asp Leu Ser Asp Val Val Pro Asn Leu Asn
                        455
```

<210> 215

<211> 315

<212> PRT

<213> Mycoplasma pneumoniae

<400> 215

Met Leu Lys Val Lys Ser Asp Phe Leu Thr Lys Asp Gln Val Ile Tyr 1 5 10 15
Asp Val Ala Ile Val Gly Ala Gly Pro Ala Gly Ile Ala Ala Gly Ile

```
20
                               25
Tyr Gly Lys Arg Ala Asn Leu Asn Leu Ala Ile Ile Glu Gly Ser Thr
                           40
Pro Gly Gly Lys Val Val Lys Thr Asn Ile Val Glu Asn Tyr Pro Gly
                      55
Tyr Lys Ser Ile Thr Gly Pro Asp Leu Gly Leu Glu Met Tyr Asn His
                  70
                                       75
Leu Ile Asp Leu Glu Pro Thr Phe Phe Tyr Ala Asn Leu Ile Lys Leu
                                   90
Asp Lys Ala Ala Asp Thr Phe Ile Leu Tyr Leu Asp Asp Lys Thr Val
                               105
Val Phe Ala Lys Thr Val Ile Tyr Ala Thr Gly Met Leu Glu Arg Lys
                           120
       115
                                               125
Leu Gly Val Ala Lys Glu Asp His Phe Tyr Gly Lys Gly Ile Ser Tyr
                       135
                                           140
Cys Ala Ile Cys Asp Gly Ser Leu Tyr Lys Asp Gln Val Val Gly Val
                                      155
Val Gly Gly Asn Ser Ala Ile Gln Glu Ala Leu Tyr Leu Ala Ser
               165
                                   170
Met Ala Lys Thr Val His Leu Ile His Arg Arg Glu Gly Phe Arg Ala
           180
                               185
Asp Glu Thr Ala Leu Asn Lys Leu Arg Asn Leu Pro Asn Val Val Phe
                          200
                                              205
His Leu Asn Tyr Thr Val Lys Glu Leu Leu Gly Asn Asn Thr Leu Asn
                      215
                                           220
Gly Ile Val Leu Gln Asn Thr Leu Asp His Ser Thr Lys Gln Ile Asp
                  230
                                     235
Leu Asn Cys Val Phe Pro Tyr Ile Gly Phe Glu Ser Ile Thr Lys Pro
              245
                                   250
                                                      255
Val Glu His Leu Asn Leu Lys Leu Asp Pro Gln Gly Phe Leu Ile Thr
                               265
Asn Glu Gln Met Glu Thr Ser Leu Lys Gly Leu Phe Ala Ala Gly Asp
                          280
Cys Arg Ser Lys His Phe Arg Gln Ile Gly Thr Ala Ile Asn Asp Gly
                      295
                            •
Ile Ile Ala Val Leu Thr Ile Arg Asp Val Leu
                   310
```

<210> 216

<211> 311

<212> PRT

<213> Mycobacterium smegmatis

<400> 216 Met Ser Thr Ser Gln Thr Val His Asp Val Ile Ile Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Ile Tyr Ala Ala Arg Ala Gln Leu Lys 20 25 Pro Leu Val Phe Glu Gly Thr Gln Phe Gly Gly Ala Leu Met Thr Thr 40 Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Glu Gly Ile Thr Gly Pro Glu Leu Met Asp Gln Met Arg Glu Gln Ala Leu Arg Phe Arg Ala Asp Leu Arg Met Glu Asp Val Asp Ala Val Gln Leu Glu Gly Pro Val Lys 85 90 Thr Val Val Val Gly Asp Glu Thr His Gln Ala Arg Ala Val Ile Leu 100 105 110 Ala Met Gly Ala Ala Ala Arg His Leu Gly Val Pro Gly Glu Glu Ala 120 125 Leu Thr Gly Met Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe 135 140 Phe Arg Asp Gln Asp Ile Val Val Gly Gly Gly Asp Ser Ala Met 150 155 Glu Glu Ala Thr Phe Leu Thr Arg Phe Ala Arg Ser Val Thr Leu Ile 170

His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile Met Leu Glu Arg Ala 185 Arg Ala Asn Glu Lys Ile Thr Phe Leu Thr Asn Thr Glu Ile Thr Gln 195 200 205 Ile Glu Gly Asp Pro Lys Val Thr Gly Val Arg Leu Arg Asp Thr Val 215 Thr Gly Glu Glu Ser Lys Leu Asp Val Thr Gly Val Phe Val Ala Ile 230 235 Gly His Asp Pro Arg Ser Glu Leu Val Arg Gly Gln Val Glu Leu Asp 245 250 Asp Glu Gly Tyr Val Lys Val Gln Gly Arg Thr Thr Tyr Thr Ser Leu 260 265 Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp His Thr Tyr Arg Gln 280 Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala Ser Ile Asp Ala Glu 295 Arg Tro Leu Ala Glu Gln Asp

<210> 217

<211> 335

<212> PRT

<213> Mycobacterium tuberculosis

<400> 217 Met Thr Ala Pro Pro Val His Asp Arg Ala His His Pro Val Arg Asp Val Ile Val Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr 20 25 Ala Ala Arg Ala Gln Leu Ala Pro Leu Val Phe Glu Gly Thr Ser Phe 40 Gly Gly Ala Leu Met Thr Thr Thr Asp Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly Ile Thr Gly Pro Glu Leu Met Asp Glu Met Arg Glu Gln 75 Ala Leu Arg Phe Gly Ala Asp Leu Arg Met Glu Asp Val Glu Ser Val 85 90 95 Ser Leu His Gly Pro Leu Lys Ser Val Val Thr Ala Asp Gly Gln Thr 100 105 110 His Arg Ala Arg Ala Val Ile Leu Ala Met Gly Ala Ala Ala Arg Tyr 120 Leu Gln Val Pro Gly Glu Gln Glu Leu Leu Gly Arg Gly Val Ser Ser 135 140 Cys Ala Thr Cys Asp Gly Phe Phe Phe Arg Asp Gln Asp Ile Ala Val 150 155 Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Thr Phe Leu Thr Arg 165 170 Phe Ala Arg Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala 180 185 190 Ser Lys Ile Met Leu Asp Arg Ala Arg Asn Asn Asp Lys Ile Arg Phe 200 205 Leu Thr Asn His Thr Val Val Ala Val Asp Gly Asp Thr Thr Val Thr 215 220 Gly Leu Arg Val Arg Asp Thr Asn Thr Gly Ala Glu Thr Thr Leu Pro 230 235 Val Thr Gly Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Gly Leu 245 250 Val Arg Glu Ala Ile Asp Val Asp Pro Asp Gly Tyr Val Leu Val Gln 265 Gly Arg Thr Thr Ser Thr Ser Leu Pro Gly Val Phe Ala Ala Gly Asp 275 280 Leu Val Asp Arg Thr Tyr Arg Gln Ala Val Thr Ala Ala Gly Ser Gly 295 Cys Ala Ala Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Ala 310 315

Thr Gly Glu Ala Asp Ser Thr Asp Ala Leu Ile Gly Ala Gln Arg

325 330 335

```
<212> PRT
<213> Neurospora crassa
<400> 218
Met His Ser Lys Val Val Ile Ile Gly Ser Gly Pro Ala Ala His Thr
                                    10
Ala Ala Ile Tyr Leu Ala Arg Ala Glu Leu Lys Pro Val Leu Tyr Glu
Gly Phe Met Ala Asn Gly Ile Ala Ala Gly Gly Gln Leu Thr Thr
                            40 .
Thr Glu Ile Glu Asn Phe Pro Gly Phe Pro Asp Gly Ile Met Gly Gln
                        55
Glu Leu Met Asp Lys Met Lys Ala Gln Ser Glu Arg Phe Gly Thr Gln
Ile Ile Ser Glu Thr Val Ala Lys Val Asp Leu Ser Ala Arg Pro Phe
                                    90
Lys Tyr Ala Thr Glu Trp Ser Pro Glu Glu Tyr His Thr Ala Asp Ser
                                105
                                                    110
Ile Ile Leu Ala Thr Gly Ala Ser Ala Arg Arg Leu His Leu Pro Gly
                            120
                                                125
Glu Glu Lys Tyr Trp Gln Asn Gly Ile Ser Ala Cys Ala Val Cys Asp
                       135
Gly Ala Val Pro Ile Phe Arg Asn Lys His Leu Val Val Ile Gly Gly
                    150
                                        155
Gly Asp Ser Ala Ala Glu Glu Ala Met Tyr Leu Thr Lys Tyr Gly Ser
                                    170
                                                        175
                165
His Val Thr Val Leu Val Arg Lys Asp Lys Leu Arg Ala Ser Ser Ile
                                185
Met Ala His Arg Leu Leu Asn His Glu Lys Val Thr Val Arg Phe Asn
                                                205
        195
                            200.
Thr Val Gly Val Glu Val Lys Gly Asp Asp Lys Gly Leu Met Ser His
                                            220
                        215
Leu Val Val Lys Asp Val Thr Thr Gly Lys Glu Glu Thr Leu Glu Ala
                    230
                                        235
Asn Gly Leu Phe Tyr Ala Ile Gly His Asp Pro Ala Thr Ala Leu Val
                                    250
Lys Gly Gln Leu Glu Thr Asp Ala Asp Gly Tyr Val Val Thr Lys Pro
                                265
Gly Thr Thr Leu Thr Ser Val Glu Gly Val Phe Ala Ala Gly Asp Val
       275
                            280
Gln Asp Lys Arg Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys
                        295
                                            300
```

<210> 218 <211> 334

310

Met Ala Ala Leu Asp Ala Glu Lys Phe Leu Ser Glu His Glu Glu Thr

Pro Ala Glu His Arg Asp Thr Ser Ala Val Gln Gly Asn Leu

<sup>&</sup>lt;210> 219

<sup>&</sup>lt;211> 333

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Penicillium chrysogenum

<sup>&</sup>lt;400> 219

Val His Ser Lys Val Val Ile Ile Gly Ser Gly Ala Gly Ala His Thr

1 10 15

Ala Ala Ile Tyr Leu Ser Arg Ala Glu Leu Gln Pro Val Leu Tyr Glu
20 25 30

Gly Met Leu Ala Asn Gly Thr Ala Ala Gly Gly Gln Leu Thr Thr
35 40 45

Thr Asp Val Glu Asn Phe Pro Gly Phe Pro Ser Gly Ile Gly Gly Ala

Glu Leu Met Asp Asn Met Arq Ala Gln Ser Glu Arq Phe Gly Thr Glu Ile Ile Thr Glu Thr Ile Ser Lys Leu Asp Leu Ser Ser Arg Pro Phe Lys Met Trp Thr Glu Trp Asn Asp Asp Glu Gly Ser Glu Pro Val Arg 105 Thr Ala Asp Ala Val Ile Ile Ala Thr Gly Ala Asn Ala Arg Arg Leu 115 120 Asn Leu Pro Gly Glu Glu Thr Tyr Trp Gln Asn Gly Ile Ser Ala Cys 135 Ala Val Cys Asp Gly Ala Val Pro Ile Phe Arg Asn Lys Pro Leu Tyr 150 155 Val Ile Gly Gly Asp Ser Ala Ala Glu Glu Ala Met Phe Leu Ala 165 170 Lys Tyr Gly Ser Ser Val Thr Val Leu Val Arg Lys Asp Lys Leu Arg 180 185 190 Ala Ser Asn Ile Met Ala Asp Arg Leu Leu Ala His Pro Lys Cys Lys 200 Val Arg Phe Asn Thr Val Ala Thr Glu Val Ile Gly Glu Asn Lys Pro 215 220 Asn Gly Leu Met Thr His Leu Arg Val Lys Asp Val Leu Ser Asn Ala 230 235 Glu Glu Val Val Glu Ala Asn Gly Leu Phe Tyr Ala Val Gly His Asp 250 Pro Ala Ser Gly Leu Val Lys Gly Gln Val Glu Leu Asp Asp Glu Gly 260 265 Tyr Ile Ile Thr Lys Pro Gly Thr Ser Phe Thr Asn Val Glu Gly Val 280 285 Phe Ala Cys Gly Asp Val Gln Asp Lys Arg Tyr Arg Gln Ala Ile Thr 295 300 Ser Ala Gly Ser Gly Cys Val Ala Ala Leu Glu Ala Glu Lys Phe Ile 310 315 Ala Glu Thr Glu Thr His Gln Glu Ala Lys Pro Val Leu 325

<210> 220 <211> 310 <212> PRT

<213> Rickettsia prowazekii

<400> 220 Met Lys Ile Thr Thr Lys Val Leu Ile Ile Gly Ser Gly Pro Ala Gly 10 Leu Ser Ala Ala Ile Tyr Thr Ala Arg Ser Ala Leu Lys Pro Ile Leu 25 Ile Asn Gly Met Gln Pro Gly Gly Gln Leu Thr Met Thr Thr Asp Val 40 45 Glu Asn Tyr Pro Gly Phe Ala Glu Thr Ile Gln Gly Pro Trp Leu Met 55 60 Glu Gln Met Ser Met Gln Ala Lys Asn Val Gly Thr Glu Ile Ile Ser 70 75 Asp Tyr Val Glu Arg Val Asp Leu Ser Lys Arg Pro Phe Lys Ile Phe 85 90 Thr Gly Thr Gly Asn Glu Tyr Glu Ala Asp Ser Ile Ile Ile Cys Thr 100 105 110 Gly Ala Glu Ser Lys Trp Leu Gly Ile Ala Ser Glu Gln Glu Phe Arg 120 125 Gly Phe Gly Val Ser Ser Cys Ala Ile Cys Asp Gly Phe Phe Phe Lys 135 140 Asn Gln Glu Ile Val Val Gly Gly Gly Asn Ser Ala Leu Glu Glu 155 Ala Leu Tyr Leu Thr Asn His Ala Asn Lys Val Thr Val Val His Arg 165 170 Arg Asn Ser Phe Arg Ala Glu Lys Ile Leu Gln Asp Arg Leu Phe Lys 185 Asn Pro Lys Ile Ser Val Ile Trp Asp His Ile Ile Asp Glu Ile Val

```
195
                           200
Gly Ser Asn Lys Pro Lys Ala Val Thr Gly Val Lys Ile Gln Asn Val
                215
                                        220
Tyr Thr Asn Glu Ile Asn Leu Val Asn Cys Ser Gly Val Phe Ile Ala
                  230
                                       235
Ile Gly His Ala Pro Asn Thr Ala Leu Phe Lys Gly Gln Ile Ala Ile
                                   250
Asp Asp Asp Asn Tyr Ile Val Thr Gln Ser Gly Ser Thr Arg Thr Asn
                                                  270
           260
                               265
Val Glu Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Ile Tyr Arg
                          280
                                              285
Gln Ala Val Thr Ala Ala Ala Ser Gly Cys Met Ala Ala Leu Glu Val
                       295
Ala Lys Phe Leu Asn Lys
```

<210> 221

<211> 322

Thr Asp

<212> PRT

<213> Schizosaccharomyces pombe

<400> 221 Met Thr His Asn Lys Val Val Ile Ile Gly Ser Gly Pro Ala Gly His Thr Ala Ala Ile Tyr Leu Ala Arg Gly Glu Leu Lys Pro Val Met Tyr 25 Glu Gly Met Leu Ala Asn Gly Ile Ala Ala Gly Gly Gln Leu Thr Thr 40 45 Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro Asp Gly Ile Asn Gly 55 Thr Thr Leu Thr Glu Asn Phe Arg Ala Gln Ser Leu Arg Phe Gly Thr 75 Glu Ile Ile Thr Glu Thr Val Ser Lys Leu Asp Leu Ser Ser Arg Pro 85 90 Phe Lys Tyr Trp Leu Glu Gly Ala Glu Glu Glu Glu Pro His Thr Ala 100 105 110 Asp Ser Val Ile Leu Ala Thr Gly Ala Ser Ala Arg Arg Leu His Ile 120 125 Thr Gly Glu Asp Thr Tyr Trp Gln Ala Gly Ile Ser Ala Cys Ala Val 135 140 Cys Asp Gly Ala Val Pro Ile Tyr Arg Asn Lys Pro Leu Ala Val Val 150 155 Gly Gly Asp Ser Ala Ala Glu Glu Ala Gln Phe Leu Thr Lys Tyr 165 170 175 Gly Ser Lys Val Tyr Val Leu Val Arg Arg Asp Lys Leu Arg Ala Ser 185 190 Pro Ile Met Ala Lys Arg Leu Leu Ala Asn Pro Lys Val Glu Val Leu 200 Trp Asn Thr Val Ala Glu Glu Ala Gln Gly Asp Gly Lys Leu Leu Asn 215 220 Asn Leu Arg Ile Lys Asn Thr Asn Thr Asn Glu Val Ser Asp Leu Gln 230 235 Val Asn Gly Leu Phe Tyr Ala Ile Gly His Ile Pro Ala Thr Lys Leu 250 Val Ala Glu Gln Ile Glu Leu Asp Glu Ala Gly Tyr Ile Lys Thr Ile 260 265 Asn Gly Thr Pro Arg Thr Ser Ile Pro Gly Phe Phe Ala Ala Gly Asp 275 280 285 Val Gln Asp Lys Val Phe Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly .295 300 Cys Gln Ala Ala Leu Leu Ala Met His Tyr Leu Glu Glu Leu Glu Asp 305

```
<211> 321
<212> PRT
<213> Streptomyces clavuligerus
Ser Asp Val Arg Asn Val Ile Ile Ile Gly Ser Gly Pro Ala Gly Tyr
                                    10
Thr Ala Ala Leu Tyr Thr Ala Arg Ala Ser Leu Gln Pro Leu Val Phe
            20
Glu Gly Ala Val Thr Ala Gly Gly Ala Leu Met Asn Thr Thr Asp Val
        35
                            40
Glu Asn Phe Pro Gly Phe Arg Asp Gly Ile Met Gly Pro Asp Leu Met
                       55
Asp Asn Met Arg Ala Gln Ala Glu Arg Phe Gly Ala Glu Leu Ile Pro
                    70
                                        75
Asp Asp Val Val Ser Val Asp Leu Thr Gly Asp Ile Lys Thr Val Thr
                85
                                    90
Asp Ser Ala Gly Thr Val His Arg Ala Lys Ala Val Ile Val Thr Thr
                                105
                                                    110
Gly Ser Gln His Arg Lys Leu Gly Leu Pro Arg Glu Asp Ala Leu Ser
                           120
        115
                                                125
Gly Arg Gly Val Ser Trp Cys Ala Thr Cys Asp Gly Phe Phe Lys
   130
                        135
                                            140
Asp Gln Asp Ile Val Val Gly Gly Gly Asp Thr Ala Met Glu Glu
                    150
                                       155
Ala Thr Phe Leu Ser Arg Phe Ala Lys Ser Val Thr Ile Val His Arg
                165
                                    170
                                                        175
Arg Asp Ser Leu Arg Ala Ser Lys Ala Met Gln Asp Arg Ala Phe Ala
           180 ·
                               185
                                                    190
Asp Pro Lys Ile Ser Phe Ala Trp Asn Ser Glu Val Ala Thr Ile His
       195
                            200
                                                205
Gly Glu Gln Lys Leu Thr Gly Leu Thr Leu Arg Asp Thr Lys Thr Gly
                        215
                                            220
Glu Thr Arg Glu Leu Ala Ala Thr Gly Leu Phe Ile Ala Val Gly His
                   230
                                      235
Asp Pro Arg Thr Glu Leu Phe Lys Gly Gln Leu Asp Leu Asp Asp Glu
                245
                                    250
                                                        255
Gly Tyr Leu Lys Val Ala Ser Pro Ser Thr Arg Thr Asn Leu Thr Gly
           260
                                265
Val Phe Ala Ala Gly Asp Val Val Asp His Thr Tyr Arg Gln Ala Ile
       275
                           280
                                               285 ·
Thr Ala Ala Gly Thr Gly Cys Ser Ala Ala Leu Asp Ala Glu Arg Tyr
                       295
                                           300
Leu Ala Ala Leu Ala Asp Ser Glu Gln Ile Ala Glu Pro Ala Pro Ala
                    310
                                       315
<210> 223
```

```
<210> 223
<211> 321
```

<210> 222

<400> 223

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Streptomyces coelicolor

```
85
                                    90
Asp Thr Ala Gly Thr Val His Arg Ala Lys Ala Val Ile Val Thr Thr
           100
                               105
Gly Ser Gln His Arg Lys Leu Gly Leu Pro Asn Glu Asp Ala Leu Ser
                          120
Gly Arg Gly Val Ser Trp Cys Ala Thr Cys Asp Gly Phe Phe Lys
                       135
Asp Gln Asp Ile Ala Val Ile Gly Gly Gly Asp Thr Ala Met Glu Glu
                                       155
                   150
Ala Thr Phe Leu Ser Arg Phe Ala Lys Ser Val Thr Ile Val His Arg
                                   170
Arg Asp Thr Leu Arg Ala Ser Lys Ala Met Gln Glu Arg Ala Phe Ala
           180
                               185
                                                   190
Asp Pro Lys Ile Ser Phe Val Trp Asp Ser Glu Val Ala Glu Val Gln
                           200
                                              205
       195
Gly Asp Gln Lys Leu Ala Gly Leu Lys Leu Arg Asn Val Lys Thr Gly
                       215
                                           220
Glu Leu Ser Asp Leu Pro Val Thr Gly Leu Phe Ile Ala Ile Gly His
                                       235
                   230
Asp Pro Arg Thr Glu Leu Phe Lys Gly Gln Leu Asp Leu Asp Pro Glu
                                   250
               245
Gly Tyr Leu Lys Val Asp Ala Pro Ser Thr Arg Thr Asn Leu Thr Gly
                                                  270
           260
                               265
Val Phe Gly Ala Gly Asp Val Val Asp His Thr Tyr Arg Gln Ala Ile
                           280
                                               285
Thr Ala Ala Gly Thr Gly Cys Ser Ala Ala Val Asp Ala Glu Pro Phe
                      295
Leu Ala Ala Leu Ser Asp Glu Asp Lys Ala Glu Pro Glu Lys Thr Ala
Val
```

<210> 224

<211> 307 <212> PRT

<213> Treponema pallidium

<400> 224 Met Glu Thr Asp Tyr Asp Val Ile Ile Val Gly Ala Gly Ala Ala Gly Leu Ser Ala Ala Gln Tyr Ala Cys Arg Ala Asn Leu Arg Thr Leu Val 25 Ile Glu Ser Lys Ala His Gly Gly Gln Ala Leu Leu Ile Asp Ser Leu 35 40 Glu Asn Tyr Pro Gly Tyr Ala Thr Pro Ile Ser Gly Phe Glu Tyr Ala 60 Glu Asn Met Lys Lys Gln Ala Val Ala Phe Gly Ala Gln Ile Ala Tyr 75 Glu Glu Val Thr Thr Ile Gly Lys Arg Asp Ser Val Phe His Ile Thr 90 85 Thr Gly Thr Gly Ala Tyr Thr Ala Met Ser Val Ile Leu Ala Thr Gly 100 105 Ala Glu His Arg Lys Met Gly Ile Pro Gly Glu Ser Glu Phe Leu Gly 120 125 Arg Gly Val Ser Tyr Cys Ala Thr Cys Asp Gly Pro Phe Phe Arg Asn 140 135 Lys His Val Val Val Ile Gly Gly Gly Asp Ala Ala Cys Asp Glu Ser 150 155 Leu Val Leu Ser Arg Leu Thr Asp Arg Val Thr Met Ile His Arg Arg 165 170 175 Asp Thr Leu Arg Ala Gln Lys Ala Ile Ala Glu Arg Thr Leu Lys Asn 185 Pro His Ile Ala Val Gln Trp Asn Thr Thr Leu Glu Ala Val Arg Gly 200 205 Glu Thr Lys Val Ser Ser Val Leu Leu Lys Asp Val Lys Thr Gly Glu

```
Thr Arg Glu Leu Ala Cys Asp Ala Val Phe Phe Ile Gly Met Val
                   230
Pro Ile Thr Gly Leu Leu Pro Asp Ala Glu Lys Asp Ser Thr Gly Tyr
                                                       255
               245
                                   250
Ile Val Thr Asp Asp Glu Met Arg Thr Ser Val Glu Gly Ile Phe Ala
           260
                                265
                                                   270
Ala Gly Asp Val Arg Ala Lys Ser Phe Arg Gln Val Ile Thr Ala Thr
                           280
Ser Asp Gly Ala Leu Ala Ala His Ala Ala Ala Ser Tyr Ile Asp Thr
  290
                       295
Leu Gln Asn
305
```

<210> 225 <211> 45 <212> PRT

<213> Vibrio fischeri

<210> 226 <211> 318 <212> PRT <213> Saccharomyces cerevisiae

<400> 226 Val His Asn Lys Val Thr Ile Ile Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Leu Ala Arg Ala Glu Ile Lys Pro Ile Leu Tyr Glu 20 25 Gly Met Met Ala Asn Gly Ile Ala Ala Gly Gly Gln Leu Thr Thr Thr 35 40 Thr Glu Ile Glu Asn Phe Pro Gly Phe Pro Asp Gly Leu Thr Gly Ser 55 60 Glu Leu Met Asp Arg Met Arg Glu Gln Ser Thr Lys Phe Gly Thr Glu Ile Ile Thr Glu Thr Val Ser Lys Val Asp Leu Ser Ser Lys Pro Phe 85 90 Lys Leu Trp Thr Glu Phe Asn Glu Asp Ala Glu Pro Val Thr Thr Asp 100 105 110 Ala Ile Ile Leu Ala Thr Gly Ala Ser Ala Lys Arg Met His Leu Pro 115 120 125 Gly Glu Glu Thr Tyr Trp Gln Lys Gly Ile Ser Ala Cys Ala Val Cys 135 140 Asp Gly Ala Val Pro Ile Phe Arg Asn Lys Pro Leu Ala Val Ile Gly 150 155 Gly Gly Asp Ser Ala Cys Glu Glu Ala Gln Phe Leu Thr Lys Tyr Gly 165 170 . 175 Ser Lys Val Phe Met Leu Val Arg Lys Asp His Leu Arg Ala Ser Thr 185 Ile Met Gln Lys Arg Ala Glu Lys Asn Glu Lys Ile Glu Ile Leu Tyr 200 205 Asn Thr Val Ala Leu Glu Ala Lys Gly Asp Gly Lys Leu Leu Asn Ala 215 220 Leu Arg Ile Lys Asn Thr Lys Lys Asn Glu Glu Thr Asp Leu Pro Val

Ser Gly Leu Phe Tyr Ala Ile Gly His Thr Pro Ala Thr Lys Ile Val

Ala Gly Gln Val Asp Thr Asp Glu Ala Gly Tyr Ile Lys Thr Val Pro

230

250

235

```
265
            260
Gly Ser Ser Leu Thr Ser Val Pro Gly Phe Phe Ala Ala Gly Asp Val
                           280
Gln Asp Ser Lys Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly Cys
                      295
Met Ala Ala Leu Asp Ala Glu Lys Tyr Leu Thr Ser Leu Glu
<210> 227
<211> 342
<212> PRT
<213> Saccharomyces cerevisiae
Met Ile Lys His Ile Val Ser Pro Phe Arg Thr Asn Phe Val Gly Ile
Ser Lys Ser Val Leu Ser Arg Met Ile His His Lys Val Thr Ile Ile
        20
                              25
Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Leu Ala Arg Ala
       35
                           40
Glu Met Lys Pro Thr Leu Tyr Glu Gly Met Met Ala Asn Gly Ile Ala
                       55
Ala Gly Gly Gln Leu Thr Thr Thr Asp Ile Glu Asn Phe Pro Gly
                                       75
                   70
Phe Pro Glu Ser Leu Ser Gly Ser Glu Leu Met Glu Arg Met Arg Lys
               85
                                   90
Gln Ser Ala Lys Phe Gly Thr Asn Ile Ile Thr Glu Thr Val Ser Lys
                              105
Val Asp Leu Ser Ser Lys Pro Phe Arg Leu Trp Thr Glu Phe Asn Glu
                           120
       115
                                               125
Asp Ala Glu Pro Val Thr Thr Asp Ala Ile Ile Leu Ala Thr Gly Ala
                       135
                                           140
Ser Ala Lys Arg Met His Leu Pro Gly Glu Glu Thr Tyr Trp Gln Gln
                                      155
                   150
Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala Val Pro Ile Phe Arg
                                   170
               165
Asn Lys Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Cys Glu Glu
          180
                               185
Ala Glu Phe Leu Thr Lys Tyr Ala Ser Lys Val Tyr Ile Leu Val Arg
                          200
                                               205
Lys Asp His Phe Arg Ala Ser Val Ile Met Gln Arg Arg Ile Glu Lys
                       215
                                           220
Asn Pro Asn Ile Ile Val Leu Phe Asn Thr Val Ala Leu Glu Ala Lys
                  230
                                     235
Gly Asp Gly Lys Leu Leu Asn Met Leu Arg Ile Lys Asn Thr Lys Ser
                                  250
              245
Asn Val Glu Asn Asp Leu Glu Val Asn Gly Leu Phe Tyr Ala Ile Gly
           260
                               265
                                                   270
His Ser Pro Ala Thr Asp Ile Val Lys Gly Gln Val Asp Glu Glu
                           280
Thr Gly Tyr Ile Lys Thr Val Pro Gly Ser Ser Leu Thr Ser Val Pro
                                           300
                       295
Gly Phe Phe Ala Ala Gly Asp Val Gln Asp Ser Arg Tyr Arg Gln Ala
                                       315
                   310
Val Thr Ser Ala Gly Ser Gly Cys Ile Ala Ala Leu Asp Ala Glu Arg
               325
                                   330
Tyr Leu Ser Ala Gln Glu
           340
<210> 228
<211> 499
<212> PRT
<213> Bos taurus
<400> 228
```

Met Asn Gly Ser Lys Asp Leu Pro Glu Pro Tyr Asp Tyr Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala Lys Tyr Asp Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 40 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Arg Asp Ser Arg Asn Tyr Gly Trp Asn Val Glu Glu Thr Val Lys His 85 90 Asp Trp Glu Arg Met Thr Glu Ala Val Gln Asn His Ile Gly Ser Leu 100 105 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Thr Tyr Glu 115 120 Asn Ala Tyr Gly Glu Phe Val Gly Pro His Arg Ile Lys Ala Thr Asn 135 140 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala 150 155 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 165 170 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 185 180 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 200 205 195 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 215 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 230 235 Gln Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val 245 250 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Ile Ala Lys 260 265 Ser Thr Asp Ser Asp Gln Thr Ile Glu Gly Glu Tyr Asn Thr Val Leu 280 Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Asn 295 300 Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Glu 315 310 Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu 325 330 Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu 345 340 Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Glu 360 365 355 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ser Cys Gly 380 375 Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Val Glu 390 395 Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg 410 Asp Asn Asn Lys Cys Tyr Ala Lys Val Val Cys Asn Ile Lys Asp Asn 420 425 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val 435 440 Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Asp Gln 455 Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr 470 475 Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asn Ile Leu Gln Thr Gly 490 Cys Cys Gly

<211> 523 <212> PRT <213> Caenorhabditis elegans

<400> 229 Met Tyr Ile Lys Gly Asn Ala Val Gly Gly Leu Lys Glu Leu Lys Ala 10 Leu Lys Gln Asp Tyr Leu Lys Glu Trp Leu Arg Asp His Thr Tyr Asp Leu Ile Val Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ser Arg Leu Gly Lys Lys Val Ala Cys Leu Asp Phe Val Lys Pro 55 60 Ser Pro Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val 70 75 Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu Gly His 85 90 Ser Ile His Asp Ala Lys Lys Tyr Gly Trp Lys Leu Pro Glu Gly Lys 105 100 Val Glu His Gln Trp Asn His Leu Arg Asp Ser Val Gln Asp His Ile 120 125 Ala Ser Leu Asn Trp Gly Tyr Arg Val Gln Leu Arg Glu Lys Thr Val 135 140 Thr Tyr Ile Asn Ser Tyr Gly Glu Phe Thr Gly Pro Phe Glu Ile Ser 150 155 Ala Thr Asn Lys Lys Lys Val Glu Lys Leu Thr Ala Asp Arg Phe 170 165 Leu Ile Ser Thr Gly Leu Arg Pro Lys Tyr Pro Glu Ile Pro Gly Val 185 180 Lys Glu Tyr Thr Ile Thr Ser Asp Asp Leu Phe Gln Leu Pro Tyr Ser 195 200 205 Pro Gly Lys Thr Leu Cys Val Gly Ala Ser Tyr Val Ser Leu Glu Cys 220 215 Ala Gly Phe Leu His Gly Phe Gly Phe Asp Val Thr Val Met Val Arg 230 235 Ser Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Glu Arg Ile Arg 245 250 Lys His Met Ile Ala Tyr Gly Met Lys Phe Glu Ala Gly Val Pro Thr 260 265 Arg Ile Glu Gln Ile Asp Glu Lys Thr Asp Glu Lys Ala Gly Lys Tyr 280 ' 275 285 Arg Val Phe Trp Pro Lys Lys Asn Glu Glu Thr Gly Glu Met Gln Glu 295 300 Val Ser Glu Glu Tyr Asn Thr Ile Leu Met Ala Ile Gly Arg Glu Ala 310 315 Val Thr Asp Asp Val Gly Leu Thr Thr Ile Gly Val Glu Arg Ala Lys 325 330 Ser Lys Lys Val Leu Gly Arg Arg Glu Gln Ser Thr Thr Ile Pro Trp 345 Val Tyr Ala Ile Gly Asp Val Leu Glu Gly Thr Pro Glu Leu Thr Pro 360 Val Ala Ile Gln Ala Gly Arg Val Leu Met Arg Arg Ile Phe Asp Gly 375 380 Ala Asn Glu Leu Thr Glu Tyr Asp Gln Ile Pro Thr Thr Val Phe Thr 390 395 Pro Leu Glu Tyr Gly Cys Cys Gly Leu Ser Glu Glu Asp Ala Met Met 405 410 Lys Tyr Gly Lys Asp Asn Ile Ile Ile Tyr His Asn Val Phe Asn Pro 425 Leu Glu Tyr Thr Ile Ser Glu Arg Met Asp Lys Asp His Cys Tyr Leu 440 445 Lys Met Ile Cys Leu Arg Asn Glu Glu Glu Lys Val Val Gly Phe His 455 460 Ile Leu Thr Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Gly Ile Ala 470 475 Leu Lys Leu Ala Ala Lys Lys Ala Asp Phe Asp Arg Leu Ile Gly Ile 490

His Pro Thr Val Ala Glu Asn Phe Thr Thr Leu Thr Leu Glu Lys Lys
500 505 510

Glu Gly Asp Glu Glu Leu Gln Ala Ser Gly Cys
515 520

<210> 230 <211> 497 <212> PRT <213> Homo sapiens

<400> 230 Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile 10 ' Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 35 40 45 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 55 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 75 Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His 90 Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 100 105 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 115 120 125 Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn 135 140 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Ser Phe Leu Ile Ala 150 155 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 165 170 175 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 180 185 190 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 195 200 205 Leu Ala Gly Ile Gly Leu Gly Val Thr Val Met Val Arg Ser Ile Leu 215 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 230 235 Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val 245 250 255 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln 265 270 Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met 280 285 Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr 295 300 Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp 310 315 Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu 325 330 Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu 340 345 Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu 360 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly 375 380 Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu 390 395 Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg 405 410 Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn 430 420 425 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val

Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln 450

Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr 465

Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly 485

Cys

<210> 231 <211> 541 <212> PRT

<213> Plasmodium falciparum

<400> 231 Met Cys Lys Asp Lys Asn Glu Lys Lys Asn Tyr Glu His Val Asn Ala Asn Glu Lys Asn Gly Tyr Leu Ala Ser Glu Lys Asn Glu Leu Thr Lys 25 Asn Lys Val Glu Glu His Thr Tyr Asp Tyr Asp Tyr Val Val Ile Gly 40 Gly Gly Pro Gly Gly Met Ala Ser Ala Lys Glu Ala Ala Ala His Gly Ala Arg Val Leu Leu Phe Asp Tyr Val Lys Pro Ser Ser Gln Gly Thr 70 Lys Trp Gly Ile Gly Gly Thr Cys Val Asn Val Gly Cys Val Pro Lys 85 90 Lys Leu Met His Tyr Ala Gly His Met Gly Ser Ile Phe Lys Leu Asp 105 Ser Lys Ala Tyr Gly Trp Lys Phe Asp Asn Leu Lys His Asp Trp Lys 120 Lys Leu Val Thr Thr Val Gln Ser His Ile Arg Ser Leu Asn Phe Ser 135 140 Tyr Met Thr Gly Leu Arg Ser Ser Lys Val Lys Tyr Ile Asn Gly Leu 150 155 Ala Lys Leu Lys Asp Lys Asn Thr Val Ser Tyr Tyr Leu Lys Gly Asp 170 Leu Ser Lys Glu Glu Thr Val Thr Gly Lys Tyr Ile Leu Ile Ala Thr 185 1.90 Gly Cys Arg Pro His Ile Pro Asp Asp Val Glu Gly Ala Lys Glu Leu 200 Ser Ile Thr Ser Asp Asp Ile Phe Ser Leu Lys Lys Asp Pro Gly Lys 215 220 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ser Gly Phe 230 235 Leu Asn Ser Leu Gly Tyr Asp Val Thr Val Ala Val Arg Ser Ile Val 245 250 Leu Arg Gly Phe Asp Gln Gln Cys Ala Val Lys Val Lys Leu Tyr Met 265 Glu Glu Gln Gly Val Met Phe Lys Asn Gly Ile Leu Pro Lys Lys Leu 280 Thr Lys Met Asp Asp Lys Ile Leu Val Glu Phe Ser Asp Lys Thr Ser 295 300 Glu Leu Tyr Asp Thr Val Leu Tyr Ala Ile Gly Arg Lys Gly Asp Ile 310 315 Asp Gly Leu Asn Leu Glu Ser Leu Asn Met Asn Val Asn Lys Ser Asn 325 330 335 Asn Lys Ile Ile Ala Asp His Leu Ser Cys Thr Asn Ile Pro Ser Ile 345 Phe Ala Val Gly Asp Val Ala Glu Asn Val Pro Glu Leu Ala Pro Val 360 Ala Ile Lys Ala Gly Glu Ile Leu Ala Arg Arg Leu Phe Lys Asp Ser 375 380 Asp Glu Ile Met Asp Tyr Ser Tyr Ile Pro Thr Ser Ile Tyr Thr Pro 395

Ile Glu Tyr Gly Ala Cys Gly Tyr Ser Glu Glu Lys Ala Tyr Glu Leu Tyr Gly Lys Ser Asn Val Glu Val Phe Leu Gln Glu Phe Asn Asn Leu 425 420 430 Glu Ile Ser Ala Val His Arg Gln Lys His Ile Arg Ala Gln Lys Asp 435 440 Glu Tyr Asp Leu Asp Val Ser Ser Thr Cys Leu Ala Lys Leu Val Cys 455 Leu Lys Asn Glu Asp Asn Arg Val Ile Gly Phe His Tyr Val Gly Pro 470 475 Asn Ala Gly Glu Val Thr Gln Gly Met Ala Leu Ala Leu Arg Leu Lys 485 490 Val Lys Lys Lys Asp Phe Asp Asn Cys Ile Gly Ile His Pro Thr Asp 500 505 Ala Glu Ser Phe Met Asn Leu Phe Val Thr Ile Ser Ser Gly Leu Ser 520 Tyr Ala Ala Lys Gly Gly Cys Gly Gly Lys Cys Gly 535

<210> 232

<211> 535

<212> PRT

<213> Arabidopsis thaliana

<400> 232 Met Ala Ala Ser Pro Lys Ile Gly Ile Gly Ile Ala Ser Val Ser Ser Pro His Arg Val Ser Ala Ala Ser Ser Ala Leu Ser Pro Pro Pro His 25 30 Leu Phe Phe Leu Thr Thr Thr Thr Thr Arg His Gly Gly Ser Tyr 40 Leu Leu Arg Gln Pro Thr Arg Thr Arg Ser Ser Asp Ser Leu Arg Leu 55 Arg Val Ser Ala Thr Ala Asn Ser Pro Ser Ser Ser Ser Gly Gly 70 75 Glu Ile Ile Glu Asn Val Val Ile Ile Gly Ser Gly Pro Ala Gly Tyr 85 90 Thr Ala Ala Ile Tyr Ala Ala Arg Ala Asn Leu Lys Pro Val Val Phe 100 105 Glu Gly Tyr Gln Met Gly Gly Val Pro Gly Gly Gln Leu Met Thr Thr 115 120 Thr Glu Val Glu Asn Phe Pro Gly Phe Pro Asp Gly Ile Thr Gly Pro 135 140 Asp Leu Met Glu Lys Met Arg Lys Gln Ala Glu Arg Trp Gly Ala Glu 150 155 Leu Tyr Pro Glu Asp Val Glu Ser Leu Ser Val Thr Thr Ala Pro Phe 165 170 Thr Val Gln Thr Ser Glu Arg Lys Val Lys Cys His Ser Ile Ile Tyr 180 185 190 Ala Thr Gly Ala Thr Ala Arg Arg Leu Arg Leu Pro Arg Glu Glu Glu 195 200 205 Phe Trp Ser Arg Gly Ile Ser Ala Cys Ala Ile Cys Asp Gly Ala Ser 215 220 Pro Leu Phe Lys Gly Gln Val Leu Ala Val Val Gly Gly Asp Thr 230 235 Ala Thr Glu Glu Ala Leu Tyr Leu Thr Lys Tyr Ala Arg His Val His 245 250 255 Leu Leu Val Arg Arg Asp Gln Leu Arg Ala Ser Lys Ala Met Gln Asp 260 265 270 Arg Val Ile Asn Asn Pro Asn Ile Thr Val His Tyr Asn Thr Glu Thr 275 280 Val Asp Val Leu Ser Asn Thr Lys Gly Gln Met Ser Gly Ile Leu Leu 295 300 Arg Arg Leu Asp Thr Gly Glu Glu Thr Glu Leu Glu Ala Lys Gly Leu

310

Phe Tyr Gly Ile Gly His Ser Pro Asn Ser Gln Leu Leu Glu Gly Gln

315

```
325
                                    330
Val Glu Leu Asp Ser Ser Gly Tyr Val Leu Val Arg Glu Gly Thr Ser
                             345
Asn Thr Ser Val Glu Gly Val Phe Ala Ala Gly Asp Val Gln Asp His
       355
                           360
                                               365
Glu Trp Arg Gln Ala Val Thr Ala Ala Gly Ser Gly Cys Ile Ala Ala
                       375
                                           380
Leu Ser Ala Glu Arg Tyr Leu Thr Ser Asn Asn Leu Leu Val Glu Phe
                   390
                                      395
His Gln Pro Gln Thr Glu Glu Ala Lys Lys Glu Phe Thr Gln Arg Asp
               405
                                   410
                                                       415
Val Gln Glu Lys Phe Asp Ile Thr Leu Thr Lys His Lys Gly Gln Tyr
           420
                                425
                                                   430
Ala Leu Arg Lys Leu Tyr His Glu Ser Pro Arg Val Ile Leu Val Leu
       435
                           440
Tyr Thr Ser Pro Thr Cys Gly Pro Cys Arg Thr Leu Lys Pro Ile Leu
                       455
                                           460
Asn Lys Val Val Asp Glu Tyr Asn His Asp Val His Phe Val Glu Ile
                   470
                                       475
Asp Ile Glu Glu Asp Gln Glu Ile Ala Glu Ala Ala Gly Ile Met Gly
               485
                                   490
Thr Pro Cys Val Gln Phe Phe Lys Asn Lys Glu Met Leu Arg Leu Gly
                               505
           500
Asn Val Leu Ser Val Leu Lys Leu His Arg Leu Leu Cys Ser Gly. Leu
    515
                           520
Ala Lys Asp Ser Glu Ser Val
  530
```

<210> 233

<211> 117

<212> PRT

<213> Helianthus annuus

<400> 233

Ala Val Val Glu Ala Tyr Gly Glu Glu Gly Lys Asn Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Ser Gly Glu Val Ser Asp Leu Lys Val 20 25 Asn Gly Leu Phe Phe Ala Ile Gly His Glu Pro Ala Thr Lys Phe Leu 35 40 Asp Gly Gln Leu Glu Leu Asp Ser Asp Gly Tyr Val Val Thr Lys Pro 50 55 Gly Thr Thr Ile Ser Ser Val Lys Gly Val Phe Ala Ala Gly Asp Val 75 Gln Asp Lys Lys Tyr Arg Gln Ala Val Thr Ala Ala Gly Ser Gly Cys 85 90 Met Ala Ala Leu Asp Ala Glu His Tyr Leu Gln Glu Ile Gly Ser Gln 100 105 Glu Gly Lys Ser Asp 115

<210> 234

<211> 300

<212> PRT

<213> Arcaeoglobus fulgidus

<400> 234

 Met Tyr Asp Val Ala Ile Ile Gly Gly Gly Pro Ala Gly Leu Thr Ala 1
 5
 10
 15

 Ala Leu Tyr Ser Ala Arg Tyr Gly Leu Lys Thr Val Phe Phe Glu Thr 20
 25
 30

 Val Asp Pro Val Ser Gln Leu Ser Leu Ala Ala Lys Ile Glu Asn Tyr 35
 40
 45

 Pro Gly Phe Glu Gly Ser Gly Met Glu Leu Leu Glu Lys Met Lys Glu 50
 55

Gln Ala Val Lys Ala Gly Ala Glu Trp Lys Leu Glu Lys Val Glu Arg 70 Val Glu Arg Asn Gly Glu Thr Phe Thr Val Ile Ala Glu Gly Glu Tyr Glu Ala Lys Ala Ile Ile Val Ala Thr Gly Gly Lys His Lys Glu 100 105 110 Ala Gly Ile Glu Gly Glu Ser Ala Phe Ile Gly Arg Gly Val Ser Tyr 120 125 Cys Ala Thr Cys Asp Gly Asn Phe Phe Arg Gly Lys Lys Val Ile Val 135 Tyr Gly Ser Gly Lys Glu Ala Ile Glu Asp Ala Ile Tyr Leu His Asp 150 155 Ile Gly Cys Glu Val Thr Ile Val Ser Arg Thr Pro Ser Phe Arg Ala 175 165 170 Glu Lys Ala Leu Val Glu Glu Val Glu Lys Arg Gly Ile Pro Val His Tyr Ser Thr Thr Ile Arg Lys Ile Ile Gly Ser Gly Lys Val Glu Lys 200 205 Val Val Ala Tyr Asn Arg Glu Lys Lys Glu Glu Phe Glu Ile Glu Ala 215 220 Asp Gly Ile Phe Val Ala Ile Gly Met Arg Pro Ala Thr Asp Val Val 230 235 Ala Glu Leu Gly Val Glu Arg Asp Ser Met Gly Tyr Ile Lys Val Asp 245 250 Lys Glu Gln Arg Thr Asn Val Glu Gly Val Phe Ala Ala Gly Asp Cys 260 265 270 Cys Asp Asn Pro Leu Lys Gln Val Val Thr Ala Cys Gly Asp Gly Ala 280 Val Ala Ala Tyr Ser Ala Tyr Lys Tyr Leu Thr Ser 295

<210> 235 <211> 315 <212> PRT

<213> Bacillus halodurans

<400> 235 Met Gly Glu Glu Gln Lys Val Tyr Asp Val Val Ile Ala Gly Ala Gly 10 Pro Ala Gly Met Thr Ala Ala Val Tyr Thr Ser Arg Ala Asn Leu Ser 20 25 Thr Val Met Val Glu Arg Gly Val Pro Gly Gly Gln Met Ala Asn Thr 40 Glu Asp Val Glu Asn Tyr Pro Gly Phe Asp His Ile Leu Gly Pro Glu 55 Leu Ser Thr Lys Met Phe Glu His Ala Lys Lys Phe Gly Ala Glu Tyr 70 75 Ala Tyr Gly Asp Ile Lys Glu Ile Ile Asp Gln Gly Asp Leu Lys Leu 85 90 Val Lys Ala Gly Asn Lys Glu Tyr Lys Ala Arg Ala Val Ile Val Ala 100 105 Thr Gly Ala Glu Tyr Lys Lys Leu Gly Val Pro Gly Glu Lys Glu Leu 120 Ser Gly Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe 135 140 Lys Gly Lys Glu Leu Val Val Val Gly Gly Gly Asp Ser Ala Val Glu 150 155 Glu Ala Val Tyr Leu Thr Arg Phe Ala Ser Lys Val Thr Ile Ile His 170 Arg Arg Asp Gln Leu Arg Ala Gln Lys Ile Leu Gln Gln Arg Ala Phe 1.85 190 Asp Asn Asp Lys Ile Glu Phe Ile Trp Asp His Val Val Lys Gln Ile 195 200 205 Asn Gly Thr Asp Gly Lys Val Ser Ser Val Thr Ile Glu His Ala Lys 215 220 Thr Gly Glu Gln Gln Asp Phe Lys Thr Asp Gly Val Phe Ile Tyr Ile

PCT/US01/50240

```
WO 02/50289
225
                   230
                                       235
Gly Met Leu Pro Leu Asn Glu Ala Val Lys Asn Leu Asn Ile Leu Asn
             245
                                 250 255
Asp Glu Gly Tyr Ile Val Thr Asn Glu Glu Met Glu Thr Ser Val Pro
           260
                              265
Gly Ile Phe Ala Ala Gly Asp Val Arg Glu Lys Ser Leu Arg Gln Ile
                           280
                                               285
Val Thr Ala Thr Gly Asp Gly Ser Leu Ala Ala Gln Asn Val Gln His
                      295
Tyr Ile Glu Glu Leu Ala Glu Lys Val Lys Asn
                   31.0
<210> 236
<211> 330
<212> PRT
<213> Bacillus halodurans
<400> 236
Met Ser Arg Lys Glu Glu Leu Tyr Asp Ile Thr Ile Ile Gly Gly Gly
Pro Thr Gly Leu Phe Ala Ala Phe Tyr Gly Gly Met Arg Gln Ala Lys
           20
Val Lys Ile Ile Glu Ser Met Pro Gln Leu Gly Gln Leu Ala Ala
       35
                           40
Leu Tyr Pro Glu Lys Tyr Ile Tyr Asp Val Ala Gly Phe Pro Lys Val
                      55
Lys Ala Gln Asp Leu Val Asn Asp Leu Lys Arg Gln Ala Glu Gln Phe
                   70
Asn Pro Thr Ile Ala Leu Glu Gln Ser Val Gln Asn Val Thr Lys Glu
              85
                                   90
Thr Asp Asp Thr Phe Thr Ile Lys Thr Asp Lys Glu Thr His Tyr Ser
                               105
Lys Ala Ile Ile Ile Thr Ala Gly Ala Gly Ala Phe-Gln Pro Arg Arg
```

120

135

215

295

150

230

310

Val Phe Pro Gly His Ser Thr Ser Leu Phe 325

165

260

Leu Glu Val Glu Gly Ala Lys Gln Tyr Glu Gly Lys Asn Leu Gln Tyr

Phe Val Asn Asp Leu Asn Ala Tyr Ala Gly Lys Asn Val Leu Ile Ser

Gly Gly Asp Ser Ala Val Asp Trp Ala Leu Met Leu Glu Pro Val

Ala Lys Asn Val Thr Leu Ile His Arg Arg Asp Lys Phe Arg Ala His 185 Glu His Ser Val Glu Leu Leu Gln Lys Ser Ser Val Asn Ile Leu Thr 200 Pro Phe Ala Ile Ser Glu Leu Ser Gly Asp Gly Glu Lys Ile His His

Val Thr Ile Gln Glu Val Lys Gly Asp Ala Val Glu Thr Leu Asp Val

Asp Glu Val Ile Val Asn Phe Gly Phe Val Ser Ser Leu Gly Pro Ile

Lys Gly Trp Gly Leu Glu Ile Glu Lys Asn Ser Ile Val Val Asn Thr

Lys Met Glu Thr Asn Ile Pro Gly Ile Tyr Ala Ala Gly Asp Ile Cys

Thr Tyr Pro Gly Lys Val Lys Leu Ile Ala Thr Gly Phe Gly Glu Ala

Pro Thr Ala Val Asn Asn Ala Lys Ala Phe Ile Asp Pro Thr Ala Arg

280

265

125

270

285

140

220

300

155

235

315

170

250

275

<sup>&</sup>lt;210> 237 <211> 213 <212> PRT <213> Bacillus halodurans

<400> 237 Met Thr Asn Leu His Tyr Thr Val Lys Ser Leu Met Arg Phe Lys Asp Lys Thr Val Ile Ile Ser Gly Gly Gly Asn Ser Ala Ile Asp Trp Ala 20 25 Asn Glu Leu Glu Pro Ile Ala Lys Lys Val Tyr Leu Thr Tyr Arg Lys 40 Glu Ala Leu Asn Gly His Glu Ala Gln Ile Ser Gln Leu Leu Ser Ser 55 Ser Ala Thr Cys Leu Phe His Thr Thr Ile Ser Lys Leu Ile Ala Arg 70 75 Asp Asn Lys Glu Val Ile Glu Gln Val Glu Leu Thr Asp His Gln Thr 85 90 Gly Glu Val Thr Asn Leu Ala Val Asp Glu Val Ile Ile Asn His Gly 100 105 Tyr Glu Arg Asp Lys Ser Leu Leu Asp Gln Ser Glu Val Thr Leu Asp 115 120 125 Arg Ile Asp Asp Tyr Tyr Ile Ala Gly Thr Pro Thr Ser Ala Thr Ser 130 135 140 Val Gly Gly Ile Tyr Ala Ala Gly Asp Val Leu Lys His Glu Gly Lys 150 155 Leu His Leu Ile Ala Gly Ala Phe Gln Asp Ala Ala Asn Ala Val Asn 165 170 Gln Ala Lys Gln Trp Ile Glu Pro Glu Ala His Gln Ser Ala Met. Val 180 185 Ser Ser His Asn His Val Phe Lys Glu Arg Asn Arg Glu Leu Ile Arg 195 200 Gln Met Leu Lys Asn 210

<210> 238

<211> 136

<212> PRT

<213> Bacillus halodurans

<400> 238

Met Asn Trp Glu Glu Leu Tyr Asp Val Thr Ile Ile Gly Gly Pro 10 Ala Gly Leu Phe Ser Ala Phe Tyr Ser Gly Leu Arg Glu Met Lys Thr 20 25 Lys Val Ile Glu Tyr Gln Pro Met Leu Gly Gly Lys Val His Val Tyr 40 Pro Glu Lys Met Ile Trp Asp Val Gly Gly Leu Thr Pro Ile Leu Gly 55 60 Glu Lys Leu Ile Glu Gln Leu Val Thr Gln Ala Leu Thr Phe Asn Pro 70 Thr Val Val Leu Asn Glu Lys Val Thr Ser Ile Ala Gln Glu Glu Ser 90 Gly Trp Phe Val Ile Arg Thr Ala Ser Gly Arg Ala His Leu Thr Lys 105 Thr Val Ile Ile Ala Val Gly Gly Ile Leu Lys Pro Gln Lys Asn 120

Arg Ala Arg Arg Gly Arg Thr Ile

<210> 239

<211> 312

<212> PRT

<213> Campylobacter jejuni

<400> 239

Lys Gly Met Pro Gly Gly Gln Ile Thr Ser Ser Glu Ile Glu Asn 40 Tyr Pro Gly Val Ala Gln Val Met Asp Gly Ile Ser Phe Met Ala Pro 55 60 Trp Ser Glu Gln Cys Met Arg Phe Gly Leu Lys His Glu Met Val Gly 75 Val Glu Gln Ile Leu Lys Asn Ser Asp Gly Ser Phe Thr Ile Lys Leu 90 85 Glu Gly Gly Lys Thr Glu Leu Ala Lys Ala Val Ile Val Cys Thr Gly 100 105 Ser Ala Pro Lys Lys Ala Gly Phe Lys Gly Glu Asp Glu Phe Phe Gly 120 125 Lys Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn 135 140 Lys Glu Val Ala Val Leu Gly Gly Gly Asp Thr Ala Leu Glu Glu Ala 145 150 155 Leu Tyr Leu Ala Asn Ile Cys Ser Lys Ile Tyr Leu Ile His Arg Arg 165 170 Asp Glu Phe Arg Ala Ala Pro Ser Thr Val Glu Lys Val Lys Lys Asn 185 Glu Lys Ile Glu Leu Ile Thr Ser Ala Ser Val Asp Glu Val Tyr Gly 195 200 205 Asp Lys Met Gly Val Ala Gly Val Lys Val Lys Leu Lys Asp Gly Ser 210 215 220 Ile Arg Asp Leu Asn Val Pro Gly Ile Phe Thr Phe Val Gly Leu Asn 230 235 Val Arg Asn Glu Ile Leu Lys Gln Asp Asp Ser Lys Phe Leu Cys Asn 250 245 Met Glu Glu Gly Gly Gln Val Ser Val Asp Leu Lys Met Gln Thr Ser 260 265 Val Ala Gly Leu Phe Ala Ala Gly Asp Leu Arg Lys Asp Ala Pro Lys 275 280 285 Gln Val Ile Cys Ala Ala Gly Asp Gly Ala Val Ala Ala Leu Ser Ala 295 Met Ala Tyr Ile Glu Ser Leu His

<210> 240 <211> 348 <212>. PRT

<213> Caulobacter crescentus

<400> 240 Met Ser Pro Leu Arg Arg Ile His Thr Ile Ser Pro Pro Met Ser Thr 10 Leu Ser Pro Arg Gln Thr Arg Cys Leu Ile Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Ile Tyr Ala Ala Arg Ala Leu Leu Lys Pro Val 40 Leu Ile Ala Gly Ile Gln Pro Gly Gly Gln Leu Thr Ile Thr Thr Asp 55 60 Val Glu Asn Tyr Pro Gly Phe Ala Asp Val Ile Gln Gly Pro Trp Leu 70 75 Met Asp Gln Met Arg Ala Gln Ala Glu His Val Gly Thr Glu Phe Val 90 Ser Asp Ile Val Thr Ser Val Asp Leu Ser Lys Arg Pro Phe Thr Val 105 Lys Thr Asp Ser Gly Gln Asp Trp Ile Ala Glu Thr Ile Ile Ile Ala 120 125 Thr Gly Ala Gln Ala Lys Trp Leu Gly Leu Glu Ser Glu Ala Lys Phe 135 Gln Gly Phe Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 155 150 Arg Asn Lys Asp Val Ile Val Val Gly Gly Gly Asn Thr Ala Val Glu 165 170 175 Glu Ala Leu Phe Leu Thr Ser Phe Ala Ser Lys Val Thr Leu Val His

```
185
            180
Arg Lys Asp Glu Leu Arg Ala Glu Lys Ile Leu Gln Glu Arg Leu Leu
                           200
Ala His Pro Lys Ile Glu Val Ile Trp Asp Ser Val Ile Asp Glu Val
                        215
                                            220
Leu Gly Gln Thr Asp Pro Met Gly Val Thr Gly Ala Arg Leu Lys Asn
                    230
                                        235
Val Lys Thr Gly Glu Thr Gln Glu Val Ala Ala Asp Gly Val Phe Ile
                245
                                   250
Ala Ile Gly His Ala Pro Ser Ser Glu Leu Phe Ala Gly Gln Leu Glu
                                265
                                                    270
Thr Gly Ser Gly Gly Tyr Leu Lys Val Lys Pro Gly Thr Ala Ser Thr
                           280
                                                285
Ala Ile Glu Gly Val Tyr Ala Ala Gly Asp Val Thr Asp Asp Val Tyr
                        295
                                            300
Arg Gln Ala Val Thr Ala Ala Gly Met Gly Cys Met Ala Ala Leu Glu
                                        315
Ala Val Arg Phe Leu Ala Glu Glu Asp His Lys Ala Ala His His Pro
               325
                                    330
Ile Ser His Ala Glu Ala Asn Lys Ile Gly Val Trp
```

<210> 241

<211> 285

<212> PRT

<213> Clostridium acetobutylicum

<400> 241 Met Glu Arg Tyr Asp Ile Ala Ile Ile Gly Ser Gly Pro Ala Gly Leu 10 Ala Ser Ala Ile Asn Ala Lys Thr Arg Asn Lys Ser Val Ile Val Phe 20 25 Gly Ser Ser Asp Leu Ser Lys Lys Leu Thr Leu Ala Pro Val Ile Asn 35 40 Asn Tyr Leu Gly Phe Tyr Gly Ile Arg Gly Ala Glu Leu Gln Glu Lys 55 Phe Lys Glu His Ile Asp Asn Met Gly Ile Gln Ile Glu Asn Val Lys 75 Val Asn Asn Ile Tyr Ala Met Gly Glu Tyr Phe Ser Ile Met Thr Ser 85 90 Lys Asp Thr Tyr Glu Ala Ser Lys Val Ile Leu Ala Met Gly Met Glu 100 105 His Thr Lys Pro Leu Lys Gly Glu Asp Lys Phe Leu Gly Arg Gly Val 120 125 Gly Tyr Cys Ala Thr Cys Asp Ala Pro Leu Tyr Lys Gly Lys Ile Val 135 140 Thr Ile Val Gly Tyr Asn Lys Glu Ala Glu Ser Glu Ala Asn Tyr Leu 150 155 Ala Glu Leu Ala Ser Lys Val Tyr Tyr Val Pro Arg Tyr Lys Asp Glu 165 170 175 Tyr Gln Leu Val Ser Ala Val Glu Ile Val Lys Asp Val Pro Val Glu 185 Ile Val Gly Asp Lys Lys Val Glu Lys Leu Lys Leu Lys Ser Arg Glu 195 205 200 Leu Glu Thr Asp Gly Val Phe Val Leu Lys Asp Ser Ala Pro Pro Glu 215 220 Gln Leu Val Pro Gly Leu Tyr Val Glu Asp Gly His Ile Lys Val Asn 230 235 Arg Lys Met Glu Thr Asn Ile Asp Gly Cys Tyr Ala Ala Gly Asp Cys 250 Thr Gly Lys Pro Tyr Gln Tyr Met Lys Ala Val Gly Glu Gly Gln Val 265 Ala Ala Leu Asn Ala Val Glu Lys Leu Tyr Thr Lys Ala

```
<210> 242
<211> 291
<212> PRT
<213> Clostridium acetobutylicum
<400> 242
Met Asp Arg Tyr Asp Ile Ala Ile Ile Gly Ser Gly Pro Ala Gly Leu
                                    10
Ser Ala Ala Ile Asn Ala Val Ile Arg Asn Lys Lys Val Ile Leu Phe
Gly Ser Asp Asn Leu Ser Asn Lys Leu Leu Lys Ala Pro Lys Ile Asn
        35
                            40
                                                45
Asn Tyr Leu Gly Ile Tyr Asp Val Ser Gly Lys Glu Leu Lys Glu Lys
   50
                        55
Phe Leu Glu His Leu Lys Tyr Met Asn Ile Glu Ile Lys Asn Glu Lys
Val Asn Ser Val Tyr Ser Met Gly Asp Tyr Phe Ala Leu Ser Leu Asn
                85
                                    90
Gln Lys Met Tyr Glu Ala Thr Ser Ile Ile Ile Ala Ser Gly Val Glu
            100
                                105
                                                    110
Phe Ser Lys Pro Leu Asn Gly Glu Asp Glu Leu Leu Gly Lys Gly Val
                            120
                                                125
Gly Tyr Cys Ala Thr Cys Asp Ala Pro Leu Tyr Lys Gly Lys Thr Val
    130
                        135
                                            140
Ala Ile Val Gly Tyr Thr Lys Glu Ala Glu Glu Ala Asn Tyr Val
                  . 150
                                        155
Ser Glu Leu Ala Gly Lys Leu Tyr Tyr Ile Pro Met Tyr Lys Asp Lys
               165
                                    170
                                                        175
Val Ser Leu Lys Glu Val Ile Glu Val Val Glu Asp Lys Pro Ile Ser
            180
                                185
                                                    190
Ile Leu Gly Lys Asp Lys Val Ser Gly Leu Gln Met Ser Lys Gly Glu
        195
                            200
                                                205
Ile Asn Thr Asp Ala Val Phe Ile Ile Lys Asp Ser Val Ser Pro Gly
   210
                        215
                                            220
Lys Leu Val Pro Gly Leu Leu Met Asn Gly Glu His Ile Ala Val Asp
                    230
                                        235
Ile Asp Met Lys Thr Asn Ile Glu Gly Cys Phe Ala Ala Gly Asp Cys
                245
                                    250
Ala Gly Arg Pro Tyr Gln Tyr Ile Lys Ser Ala Gly Gln Gly Gln Ile
            260
                                265
                                                    270
Ala Ala Leu Ser Ala Val Ser Tyr Ile Asp Lys Ile Lys Leu Asn Lys
        275
                            280
                                                285
Lys Ile Ile
    290
<210> 243
<211> 314
<212> PRT
<213> Clostridium sticklandii
<400> 243
Met Ser Lys Ile Tyr Asp Leu Val Ile Ile Gly Ala Gly Pro Ala Gly
                                    10
Leu Ser Ala Gly Leu Tyr Gly Ala Arg Gly Lys Met Ser Thr Leu Ile
           20
                                25
Ile Glu Lys Asp Lys Thr Gly Gly Gln Ile Val Thr Thr Glu Glu Val
                            40
                                                45
Ala Asn Tyr Pro Gly Ser Ile His Asp Ala Ser Gly Pro Ser Leu Ile
                       55
                                            60
Ala Arg Met Ala Glu Gln Ala Asp Glu Phe Gly Thr Glu Arg Ile Lys
                    70
                                       75
Asp Ser Ile Val Asp Phe Asp Phe Thr Gly Lys Ile Lys Leu Lys
                85
                                    90
```

Gly Thr Lys Ala Glu Tyr Gln Ala Lys Ala Val Ile Val Ala Thr Gly
100 105 110

Ala Ser Pro Lys Lys Leu Asp Cys Pro Gly Glu Lys Glu Leu Thr Gly

```
120
                                               125
       115
Lys Gly Val Ser Tyr Cys Ala Thr Cys Asp Ala Asp Phe Phe Gln Asp
                      135
                                       140
Met Glu Val Phe Val Val Gly Gly Asp Ser Ala Val Glu Glu Ala
                   150
                                       155
Met Tyr Leu Thr Lys Phe Ala Ser Lys Val Thr Ile Val His Arg Arg
                                   170
              165
Asp Ser Leu Arg Ala Ala Lys Ser Ile Gln Asp Lys Ala Phe Ala Asn
                              185
Pro Lys Ile Asp Phe Lys Trp Asp Ser Val Ile Lys Glu Ile Lys Gly
       195
                           200
Asp Gly Ile Val Glu Ser Val Val Phe Glu Asn Thr Lys Thr Gly Glu
                                          220
                      215
Leu Ser Glu His Phe Ala Asp Glu Glu Phe Gly Thr Phe Gly Ile Phe
                                      235
                  230
Val Phe Thr Gly Tyr Ile Pro Gln Thr Asp Ile Phe Lys Asp Lys Val
                                   250
               245
Asp Met Asn Gln Ser Gly Tyr Phe Val Thr Asn Gln Asn Met Glu Thr
           260
                               265
Asn Ile Pro Gly Val Phe Ala Ala Gly Asp Cys Arg Glu Lys Val Leu
                                               285
       275
                           280
Arg Gln Val Val Thr Ala Thr Ala Asp Gly Ala Ile Ala Ala Ile Met
                       295
                                          300
Ala Glu Lys Tyr Ile Glu His Glu Gly Leu
```

<210> 244

<211> 325

<212> PRT

<213> Deinococcus radiodurans

<400> 244 Met Thr Ala Pro Thr Ala His Asp Tyr Asp Val Val Ile Ile Gly Gly 10 Gly Pro Ala Gly Leu Thr Ala Ala Ile Tyr Thr Gly Arg Ala Gln Leu Ser Thr Leu Ile Leu Glu Lys Gly Met Pro Gly Gly Gln Ile Ala Trp 40 Ser Glu Glu Val Glu Asn Phe Pro Gly Phe Pro Glu Pro Ile Ala Gly 55 Met Glu Leu Ala Gln Arg Met His Gln Gln Ala Glu Lys Phe Gly Ala 70 75 Lys Val Glu Met Asp Glu Val Gln Gly Val Gln His Asp Ala Thr Ser 90 His Pro Tyr Pro Phe Thr Val Arg Gly Tyr Asn Gly Glu Tyr Arg Ala 100 105 Lys Ala Val Ile Leu Ala Thr Gly Ala Asp Pro Arg Lys Leu Gly Ile 125 115 120 Pro Gly Glu Asp Asn Phe Trp Gly Lys Gly Val Ser Thr Cys Ala Thr 135 140 Cys Asp Gly Phe Phe Tyr Lys Gly Lys Lys Val Val Ile Gly Gly 150 155 Gly Asp Ala Ala Val Glu Glu Gly Met Phe Leu Thr Lys Phe Ala Asp 170 165 Glu Val Thr Val Ile His Arg Arg Asp Thr Leu Arg Ala Asn, Lys Val 180 185 Ala Gln Ala Arg Ala Phe Ala Asn Pro Lys Met Lys Phe Ile Trp Asp 200 205 Thr Ala Val Glu Glu Ile Gln Gly Ala Asp Ser Val Ser Gly Val Lys 215 Leu Arg Asn Leu Lys Thr Gly Glu Val Ser Glu Leu Ala Thr Asp Gly 230 235 Val Phe Ile Phe Ile Gly His Val Pro Asn Thr Ala Phe Val Lys Asp 245 250 255 Thr Val Ser Leu Arg Asp Asp Gly Tyr Val Asp Val Arg Asp Glu Ile 265

<210> 245 <211> 61 <212> PRT <213> Enterococcus faecalis <220> <221> VARIANT <222> 33, 45, 46 <223> Xaa = Any Amino Acid

<210> 246 <211> 205 <212> PRT <213> Halobacterium sp

<400> 246 Met Thr Glu Asp Ser His Asp Leu Val Ile Ala Gly Ser Gly Ile Ala 10 Gly Leu Ser Ala Ala Val Tyr Ala Ala Arg Ala Asp Leu Glu Pro Leu 20 25 Val Leu Glu Gly Asp Glu Pro Gly Gly Gln Leu Thr Leu Thr Thr Asp 40 Val Glu Asn Tyr Leu Gly Phe Pro Asp Gly Val Gly Gly Met Asp Leu Val Gln Arg Gly Lys Glu Gln Ala Glu Gln Phe Gly Ala Gln Phe Glu 70 His Gly Arg Ile Glu Ala Ala Asp Leu Asp Gly Gln Pro Leu Glu Leu 90 Ser Leu Ser Thr Gly Asp Thr Leu Tyr Thr Arg Ser Leu Ile Val Ala 105 Thr Gly Ala Ser Ala Arg Trp Val Gly Ala Glu Asn Glu Asp Glu Leu 120 Met Gly Ala Gly Leu Ser Thr Cys Ala Thr Cys Asp Gly Ala Phe His 130 140 135 Arg Gly Asp Asp Val Leu Val Val Gly Gly Asp Ser Ala Met Glu 150 155 Glu Ala Leu Phe Leu Ala Lys Phe Ala Asp Ser Val Thr Val Val His 170 175 Arg Arg Glu Glu Leu Arg Ala Ser Glu Ile Met Ala Asp Arg Ala Arg 185 Asp His Asp Asp Val Gln Phe Arg Trp Asn Thr Glu Leu 195 200

<210> 247 <211> 362

<212> PRT <213> Halobacterium sp

<400> 247 Met Thr Glu Ala Thr Ala Asp Arg Thr Ala Leu Thr Asp Gly Gly Arg Asp Val Val Glu His Arg Gln Leu Val Ile Val Gly Ser Gly Ile Ala 20 Ala Leu Ser Ala Ala Thr Tyr Ala Ala Arg Ser Asn Asn Asp Pro Leu 35 40 45 Leu Phe Glu Gly Asp Glu Pro Gly Gly Gln Leu Thr Leu Thr Ser Glu Val Glu Asn Tyr Pro Gly Phe Pro Glu Gly Ile Ala Gly Ala Glu Leu 70 Ile Gln Glu Met Lys Thr Gln Ala Thr Arg Phe Gly Ala Glu Val Glu 85 90 His Gly Ile Val Glu Ser Val Asp Asp Ser Gly Arg Pro Phe Arg Leu 105 110 Thr Leu Thr Asn Gly Asp Val Tyr Thr Ala Asp Ala Val Ile Val Ala 115 120 Ser Gly Ala Ser Ala Arg Thr Leu Gly Ile Pro Gly Glu Asp Glu Leu 135 140 Met Gly Gln Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Ala Phe Phe 150 155 Arg Gly Glu Asp Met Ile Val Val Gly Gly Asp Ala Ala Glu 165 170 175 · Glu Ala Ser Phe Leu Thr Lys Phe Ala Asp Thr Val Tyr Leu Val His 1.80 185 190 Arg Arg Asp Glu Leu Arg Ala Glu Asp Tyr Trp Ala Asp Arg Ile Arg 195 200 205 Glu His Val Ala Asp Gly Asp Ile Glu Val Leu Trp Asn Thr Glu Ala 215 220 Val Glu Val His Gly Ser Pro Glu Glu Gly Val Thr Gly Ala Ser Leu 230 235 Val Arg His Pro Glu Gly His Pro Thr Ala Lys Leu Asp Ala Asp Glu 245 250 Thr Glu Gln Leu Glu Leu Asp Ile Gly Ala Phe Phe Ile Ala Ile Gly 260 265 270 His Thr Pro Asn Thr Ser Phe Leu Ala Asp Thr Gly Val Val Cys Asp 275 280 Asp Ala Gly Tyr Val Gln Thr Val Gly Gly Ala Gly Gly Gln Thr 295 300 Lys Thr Asp Val Thr Gly Val Phe Gly Ala Gly Asp Val Val Asp Tyr 310 315 320 His Tyr Gln Gln Ala Val Thr Ala Ala Gly Met Gly Ser Lys Ala Ala 325 330 Ile Asp Ala Asp Glu Tyr Leu Glu Ser Val Ala Asp Gly Val Thr Gly 345 Glu Thr Ala Asp Ala Thr Pro Ala Asp Asp

<210> 248 <211> 294 <212> PRT

<213> Halobacterium

```
70
Ile Ala Asp Thr Val Glu Ser Val Asp Arg Pro Ser Asp Asp Asp Thr
                                   90
Gly Phe Val Val Glu Thr Gln Asp Gly Arg Arg Val Tyr Thr Asp Thr
           100
                               105
                                                   110
Val Leu Ala Ala Ala Trp Tyr Asp Gly Ser Tyr Leu Arg Pro Val Val
                           120
                                                125
Gly Asp Ser Ala Phe Glu Thr His Asp His His Gly Glu Ser Arg Glu
                        135
                                           140
Arg Phe Asp Asp Ala Tyr Ala Asp Ala Asp Gly Arg Thr Pro Val Asp
                   150
                                       155
Gly Leu Tyr Val Ala Ser Pro Gly Gly Gln Arg Ser Ala Gln Ala Val
                                   170
               165
Ile Ala Ala Gly Asn Gly Ala His Val Ala Arg Cys Leu Leu Ala Asp
           180
                               185
Arg Lys Arg Ala Arg Gly Tyr Pro Glu Gly Val Ala Pro His Tyr Asp
       195
                           200
Trp Lys Arg Arg Glu Ser Asp Leu Ser Gly Glu Trp Ala Asp Arg Asp
   210
                       215
                                           220
Arg Trp Arg Glu Trp Phe Ala Ala Glu Ala Gly Asp Asp His Asp Leu
                   230
                                       235
Asp Asp Asp Glu Phe Ala Ala Leu Arg Ala Ala His Leu Asp Arg Thr
               245
                                   250
Phe Asp Ala Thr Leu Ser Ala Asp Ala Ile Glu Glu Arg Ala Glu Ala
                               265
           260
Gly Ala His Arg Leu Leu Asp His Ile Asp Asp Asp His Ile Glu Ser
                           280
Tyr Arg Glu Gln Arg Asp
   290
```

<210> 249

<211> 324

<212> PRT

<213> Helicobacter pylori

Met Asn Gln Glu Ile Leu Asp Val Leu Ile Val Gly Ala Gly Pro Gly Gly Ile Ala Thr Ala Val Glu Cys Glu Ile Ala Gly Val Lys Lys Val Leu Leu Cys Glu Lys Thr Glu Ser His Ser Gly Met Leu Glu Lys Phe Tyr Lys Ala Gly Lys Arg Ile Asp Lys Asp Tyr Lys Lys Gln Val Val Glu Leu Lys Gly His Ile Pro Phe Lys Asp Ser Phe Lys Glu Glu Thr Leu Glu Asn Phe Thr Asn Leu Leu Lys Glu His His Ile Thr Pro Ser Tyr Lys Thr Asp Ile Glu Ser Val Lys Lys Glu Gly Glu Tyr Phe Lys Ile Thr Thr Thr Ser Asn Thr Thr Tyr His Ala Lys Phe Val Val Val Ala Ile Gly Lys Met Gly Gln Pro Asn Arg Pro Thr Ala Tyr Lys Ile Pro Val Ala Leu Ser Lys Gln Val Val Phe Ser Ile Asn Asp Cys Lys Glu Asn Glu Lys Thr Leu Val Ile Gly Gly Gly Asn Ser Ala Val Glu Tyr Ala Ile Ala Leu Cys Lys Thr Thr Pro Thr Thr Leu Asn Tyr Arg 180 ' Lys Lys Glu Phe Ser Arg Ile Asn Glu Asp Asn Ala Lys Asn Leu Gln Glu Val Leu Asn Asn Asn Thr Leu Lys Ser Lys Leu Gly Val Asp Ile Glu Ser Leu Glu Glu Asp Asn Thr Gln Ile Lys Val Asn Phe Thr Asp 

<210> 250

<211> 128

<212> PRT

<213> Klebsiella oxytoca

<400> 250

Met Gly Thr Ala Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro 10 Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro 20 Val Leu Ile Thr Gly Met Glu Lys Gly Gln Leu Thr Thr Thr Thr 35 . 40 45 Glu Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu 55 60 Leu Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile 70 75 Ile Phe Asp His Ile Asn Ser Val Asp Leu Gln Asn Arg Pro Phe Arg 90 Leu Val Gly Asp Ser Gly Glu Tyr Thr Cys Asp Ala Pro Asp Tyr Arg 100 105 110 Tyr Arg Arg Ile Ser Ala Leu Ser Gly Ser Ala Ile Gly Arg Arg Val 115 120 125

<210> 251

<211> 79

<212> PRT

<213> Lactococcus lactis

<400> 251

 Met Gln Glu Leu Asp Leu Ile Ile Val Gly Ala Gly Pro Val Gly Leu 1
 5
 10
 15

 Tyr Ala Ala Phe Tyr Ala Gly Met Arg Gly Leu Ser Val Ala Ile Ile 20
 25
 30

 Glu Ser Ala Gln Val Pro Gly Gly Gln Pro Gln Asn Leu Tyr Pro Glu 35
 40
 45

 Lys Leu Ile Tyr Asp Ile Ala Gly Leu Pro Ala Val Thr Gly Ala Asp 50
 55
 60

 Leu Thr Lys Asn Leu Leu Glu Gln Leu Ala Gln Ile Ser His Arg 65
 70
 75

<210> 252

<211> 321

<212> PRT

<213> Lactococcus lactis

<400> 252

Met Gln Glu Leu Asp Leu Ile Ile Val Gly Ala Gly Pro Val Gly Leu 1 5 10 15

Tyr Ala Ala Phe Tyr Ala Gly Met Arg Gly Leu Ser Val Ala Ile Ile 20 25 30

Glu Ser Ala Gln Val Pro Gly Gly Gln Pro Gln Asn Leu Tyr Pro Glu

```
40
Lys Leu Ile Tyr Asp Ile Ala Gly Leu Pro Ala Val Thr Gly Ala Asp
                       55
Leu Thr Lys Asn. Leu Leu Glu Gln Leu Ala Gln Ile Ser His Arg Leu
Phe Leu Gly Glu Ser Val Gln Lys Ile Glu Lys Glu Glu Gly Ile Phe
                                   90
Ser Val Thr Thr Asp Lys Ser Thr Arg Arg Ala Lys Gly Val Leu Leu
                               105
Thr Thr Gly Ala Gly Leu Leu Lys Pro Arg Lys Leu Gly Ile Asp Asn
                                               125
                           120
Glu Glu Thr Leu Ala Asn Glu Gly Lys Ile Ser Tyr Phe Ile Thr Ser
                       135
                                           140
Leu Lys Glu Phe Glu Gly Lys Asn Val Ala Val Phe Gly Gly Asp
                                       155
                   150
Ser Ala Leu Asp Trp Ser Leu Met Leu Glu Lys Val Ala Lys Asn Val
                                  170
               165
His Leu Val His Arg Arg Thr Ala Phe Arg Gly His Glu Ile Thr Val
                               185
Asp Arg Val Met Asn Ser Asn Val Gln Val His Thr Pro Tyr Thr Phe
                           200
                                               205
Ser Asn Leu Ile Glu Asn Glu Leu Glu Leu Lys Lys Ile Lys Ser Glu
                                          220
                      215
Glu Ser Leu Asn Phe Ser Ile Asp Lys Ile Leu Val Asn Tyr Gly Phe
                                      235
                   230
Leu Thr Asn Gln Val Thr Leu Ala Glu Asn Leu Glu Val Ser Arg Asn
                                   250
Gly Arg Val Lys Ala Asp Ser Met Met Gln Ser Asn Ile Glu Gly Leu
          260
                            265
Tyr Val Ala Gly Asp Ala Ser Asp Tyr Pro Gly Lys Met Pro Leu Met
       275
                           280
Ser Val Gly Phe Gly Glu Ala Val His Ala Ile Asn Ala Met Thr Lys
                                           300
                       295
Lys Leu Glu Phe Asp His Pro Leu Arg Gly Gly His Ser Ser Ser Ile
```

<210> 253

<211> 308

<212> PRT

<213> Lactococcus lactis

Met Thr Glu Lys Lys Tyr Asp Val Val Ile Ile Gly Ser Gly Pro Ala 10 Gly Met Thr Ala Ala Met Tyr Thr Ala Arg Ser Glu Met Lys Thr Leu Leu Leu Glu Arg Gly Val Pro Gly Gly Gln Met Asn Asn Thr Ala Glu Ile Glu Asn Tyr Pro Gly Tyr Glu Thr Ile Met Gly Pro Glu Leu Ser 55 Met Lys Met Ala Glu Pro Leu Glu Gly Leu Gly Val Glu Asn Ala Tyr 75 70 Gly Phe Val Thr Ala Ile Glu Asp His Gly Asp Tyr Lys Lys Ile Ile 90 Thr Glu Asp Asp Glu Phe Val Thr Lys Ser Ile Ile Ile Ala Thr Gly 105 Ala Asn His Arg Lys Leu Glu Ile Pro Gly Glu Glu Glu Tyr Gly Ala 125 115 120 Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Arg Asn 135 140 Gln Glu Ile Leu Val Ile Gly Gly Gly Asp Ser Ala Val Glu Glu Ala 150 155 Leu Tyr Leu Thr Arg Phe Gly Gln Ser Val Thr Ile Met His Arg Arg 170

Asp Lys Leu Arg Ala Gln Glu Ile Ile Gln Gln Arg Ala Phe Lys Glu 185 Glu Lys Ile Asn Phe Ile Trp Asp Ser Val Pro Met Glu Ile Lys Gly 195 200 205 Asp Asp Lys Lys Val Gln Ser Val Val Tyr Lys Asn Val Lys Thr Gly 210 215 220 Glu Val Thr Glu Lys Ala Phe Gly Gly Ile Phe Ile Tyr Val Gly Leu 230 235 Asp Pro Val Ala Glu Phe Ala Gly Asn Leu Gly Ile Thr Asp Glu Ala 245 250 255 Gly Trp Ile Ile Thr Asp Asp His Met Arg Thr Ser Leu Pro Gly Ile 260 265 Phe Ala Val Gly Asp Val Arg Gln Lys Asp Phe Arg Gln Ile Thr Thr 280 Ala Ile Gly Asp Gly Ala Gln Ala Gln Glu Ala Tyr Lys Phe Val 295 Ala Glu Leu Asp 305

<210> 254

<211> 44

<212> PRT

<213> Lactococcus lactis

<400> 254

Met Gln Glu Leu Asp Leu Ile Ile Val Gly Ala Gly Pro Val Gly Leu

1 5 10 15

Tyr Ala Ala Phe Tyr Ala Gly Met Arg Gly Leu Ser Val Ala Ile Ile
20 25 30

Glu Ser Ala Gln Val Pro Gly Gly Gln Pro Gln Asn
35 40

<210> 255

<211> 339

<212> PRT

<213> Listeria monocytogenes

<400> 255

Glu Phe Tyr Ser Tyr Lys Lys Glu Ile Asn Arg Tyr Leu Ala Glu Glu 10 Asp Ser Ala Ser Ala Cys Asp Ile Leu Arg Lys Val Ile Asp Glu Lys 20 25 Pro Asn Phe Trp Pro Ala Tyr Asn Gln Leu Ala Ser Leu Tyr Phe Glu 35 40 45 Gln Leu Lys Glu Glu Gly Val Arg Val Leu Ser Asp Leu Leu Ser 55 Arg Asn Pro Gly Asn Leu Leu Gly Ile Cys Asp Leu Phe Ile Tyr His Phe Tyr Lys Gly Asn Arg Lys Glu Ala Asp Glu Leu Tyr Leu Glu Leu 90 Arg Asp Val Leu Pro Val Leu Ala His His Lys Glu Lys Leu Gly Leu 100 105 Ile His Ala Met Met Gly Glu Tyr Glu Glu Ala Asp Asp Leu Leu Glu 115 120 125 Gln Val Ala Asp Leu Glu Val Thr Glu Arg Ser Lys Tyr Tyr Phe 135 140 Arg Ala Lys Ser Ser Tyr Tyr Leu Gly Asp Val Glu Gly Ala Lys Met 145 150 155 Phe Trp His Ser Phe Leu Glu Cys Asp Leu Tyr Glu Asp Val Arg Phe 165 170 175 Pro Trp Glu Gln Glu Pro Asp Leu Thr Asn Asp Thr Arg Leu Val Leu 185 Glu Met Leu Gln Glu Glu Asp Asp Leu Thr His Met Leu Gly Val Tyr 200 205 Ala Leu Thr Ile Ser Gly Asn Arg Pro Glu Leu Val Leu Phe His Pro

```
215
Leu Leu Asp Met Ser Asp Trp Ser Tyr Met Glu His Leu Met Phe Thr
                 230
                                      235
Asn Phe Asp Tyr Phe Pro Asp Gly Ala Ile Glu Gln Asn Gly Tyr Leu
                               250
              245
Ile Ala Lys Ala Met Ile Ile Leu Lys Glu Asn Gly Ile Leu Leu Asn
           260
                           265
Glu Glu Tyr Met Ala Leu Tyr Lys Gln Met Phe Ser Leu Val Leu Ile
       275
                          280
Asp Ala Gly Lys Asp Leu Ile Leu Gly Arg Tyr Thr Ile Glu Thr Val
                     295
                                         300
Ala Ser Ala Ile Ala Lys Leu Phe Leu Pro His Leu Lys Leu Gln Leu
                  310
                                     315
Val Glu Glu Phe Glu Cys Ser Lys Cys Ala Arg Asp Ile Glu Arg Val
                                  330
Leu Ser Arg
```

<210> 256 <211> 303 <212> PRT

<213> Methanothermobacter thermautotrophicus

<400> 256 Met Met Thr Asp Tyr Asp Met Ile Val Ile Gly Ala Gly Pro Ala Gly Leu Thr Ala Gly Ile Tyr Gly Gly Arg Gln Gly Ser Ser Val Leu Met Leu Asp Lys Gly Pro Ala Gly Gly Leu Gly Leu Glu Val Pro Met Met 35 40 Glu Asn Tyr Pro Gly Phe Glu Met Ile Ala Gly Met Ser Leu Val Thr 55 Lys Met Lys Lys Gln Ala Thr Ala Val Ala Glu Leu Arg Glu Met Glu . 70 75 Glu Val Lys Glu Ile Glu Lys Gly Asp Val Phe Thr Val Lys Thr Ser 85 90 Arg Asp Thr Tyr Thr Ala Ser Ala Ile Ile Phe Ala Thr Gly Ser Lys 100 105 110 His Arg Gln Leu Gly Val Pro Gly Glu Asn Asp Leu Leu Gly Arg Gly 120 125 115 Val Cys Tyr Cys Ala Thr Cys Asp Gly Pro Leu Tyr Lys Gly Arg Lys 130 135 Val Leu Met Val Gly Gly Asn Ser Ala Ala Gln Glu Ala Val Phe 150 155 Leu Lys Asn Ile Gly Cys Asp Val Ser Ile Val His Arg Arg Asp Glu 170 165 175 Leu Arg Ala Asp Lys Tyr Leu Gln Asp Lys Leu Arg Glu Met Glu Ile 180 185 Pro Val Ile Trp Asn Ser Val Val Lys Glu Ile Gly Gly Asp Glu Arg 200 205 Val Glu Glu Val Ile Ile His Asn Arg Val Thr Gly Arg Asp Glu Thr 215 220 Leu Lys Val Asp Gly Val Phe Ile Ala Ile Gly Glu Glu Pro Leu Asn 230 235 Gln Leu Ala Val Asp Leu Gly Val Glu Val Asp Lys Gly Gly Tyr Ile 245 250 255 Ile Thr Asp Lys Phe Gln Arg Thr Asn Val Pro Leu Val Tyr Ala Ala 265 Gly Asp Ile Thr Gly Gly Leu Asn Gln Trp Val Thr Ala Cys Ala Glu 275 280 285 , Gly Ala Ile Ala Ala Thr Tyr Ala Tyr Arg Glu Ile Gln Ser Tyr 295

<210> 257 <211> 179

<212> PRT <213> Bacillus subtilis

<400> 257 Met Val Ile Ser Gly Gly Gly Asp Thr Ala Val Asp Trp Ala Asn Glu Leu Glu Pro Ile Ala Ala Ser Val Thr Val Val His Arg Arg Glu Glu 20 25 Phe Gly Gly Met Glu Ser Ser Val Thr Lys Met Lys Gln Ser Ser Val 35 40 Arg Val Leu Thr Pro Tyr Arg Leu Glu Gln Leu Asn Gly Asp Glu Glu 55 Gly Ile Lys Ser Val Thr Val Cys His Thr Glu Ser Gly Gln Arg Lys Asp Ile Glu Ile Asp Glu Leu Ile Ile Asn His Gly Phe Lys Ile Asp 85 90 Leu Gly Pro Met Met Glu Trp Gly Leu Glu Ile Glu Glu Gly Arg Val 105 Lys Ala Asp Arg His Met Arg Thr Asn Leu Pro Gly Val Phe Val Ala 115 120 125 Gly Asp Ala Ala Phe Tyr Glu Ser Lys Leu Arg Leu Ile Ala Gly Gly 135 140 Phe Thr Glu Gly Pro Thr Ala Val Asn Ser Ala Lys Ala Tyr Leu Asp 150 155 Pro Lys Ala Glu Asn Met Ala Met Tyr Ser Thr His His Lys Lys Leu 170 Val His Lys

<210> 258 <211> 307 <212> PRT <213> Mycoplasma pulmonis

180

<400> 258

Met Ser Gln Asn Lys Ile Tyr Asp Val Ala Ile Ile Gly Ala Gly Pro 10 Gly Ala Leu Thr Ala Ala Ile Tyr Thr Ser Arg Gly Asn Leu Asp Thr 25 Val Phe Ile Asp Asn Ala Ala Pro Gly Gly Lys Leu Ile Tyr Ala Ser 40 Lys Ile Glu Asn Trp Pro Gly Asp Thr Ile Val Lys Gly Thr Asp Leu 55 Ala Ile Arg Phe Phe Glu His Ala Gln Ala Phe Gly Ala Lys Tyr Glu 70 75 Tyr Gly Lys Val Val Asp Leu Ile Asn Ile Lys Asp Asp Leu Lys Glu 85 Leu Val Leu Glu Asp Gly Lys Lys Ile Gln Ala Lys Ser Val Ile Ile 105 110 Ala Ser Gly Met Val Ser Arg Lys Pro Arg Glu Ile Leu Asn Tyr Asp 120 125 Glu Phe Glu Asn Arg Gly Val Ser Tyr Cys Val Ile Cys Asp Gly Pro 130 135 140 Met Tyr Gly His Asn Pro Ala Ile Ile Ile Gly Gly Gly Asn Ser Ala 150 155 Val Glu Glu Gly Thr Phe Leu Ser Ser Ile Ala Ser Lys Val Tyr Val 170 165 175

Ile Val Arg Asp Ser Asp Phe Ile Ala Glu Lys Ala Leu Val Asn Asp

Leu Lys Ser Arg Lys Asn Ile Glu Val Leu Phe Asn Ala Ser Val Lys 195 200 205 Glu Leu His Gly Lys Asp Ala Leu Glu Tyr Ala Ile Val Asn His Asn

Cly Lys Glu Val Lys Leu Glu Val Ala Ser Leu Phe Pro Tyr Ile Gly

215

185

190

235

```
245
                                   250
Asn Gly Phe Ile Lys Thr Asp Glu Phe Met Glu Thr Lys Val Pro Gly
            260
                           265
                                             270
Ile Tyr Ala Ile Gly Asp Ile Arg Ile Lys Asp Ile Arg Gln Ile Leu
                           280
Thr Ala Thr Ser Asp Gly Thr Ile Ala Gly Lys Ile Leu Thr Asn Arg
                                            300
Ile Lys Lys
305
<210> 259
<211> 316
<212> PRT
<213> Neisseria meningitidis
<400> 259
Met Ser Gln His Arg Lys Leu Ile Ile Leu Gly Ser Gly Pro Ala Gly
Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Asn Pro Val Ile
          20
                                25
Ile Thr Gly Ile Ala Gln Gly Gln Leu Met Thr Thr Glu Val
       35
                           40
                                             . 45
Asp Asn Trp Pro Ala Asp Ala Asp Gly Val Gln Gly Thr Glu Leu Met
Ala Arg Phe Leu Ala His Ala Glu Arg Phe Gly Thr Glu Ile Ile Phe
                   70
                                       75
Asp Gln Ile Asn Ala Val Asp Leu Gln Lys Arg Pro Phe Thr Leu Lys
               85
                                  90
Gly Asp Met Gly Glu Tyr Thr Cys Asp Ala Leu Ile Val Ala Thr Gly
            100
                               105
Ala Ser Ala Lys Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe Ala Gly
                           120
Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn
                                           140
                       135
Gln Asp Val Ala Val Val Gly Gly Asn Thr Ala Val Glu Glu Ala
                   150
                                       155
Leu Tyr Leu Ala Asn Ile Ala Lys Thr Val Thr Leu Ile His Arg Arg
               165
                                   170
Ser Glu Phe Arg Ala Glu Lys Ile Met Ile Asp Lys Leu Met Lys Arg
           180
                               185
Val Glu Glu Gly Lys Ile Ile Leu Lys Leu Glu Ser Asn Leu Gln Glu
                                               205
                          200
Val Leu Gly Asp Asp Arg Gly Val Asn Gly Ala Leu Leu Lys Asn Asn
                       215
                                           220
Asp Gly Ser Glu Gln Gln Ile Ala Val Ser Gly Ile Phe Ile Ala Ile
                   230
                                       235
Gly His Lys Pro Asn Thr Asp Ile Phe Lys Gly Gln Leu Glu Met Asp
               245
                                  250
Glu Ala Gly Tyr Leu Lys Thr Lys Gly Gly Thr Ala Asp Asn Val Gly
           260
                               265
Ala Thr Asn Ile Glu Gly Val Trp Ala Ala Gly Asp Val Lys Asp His
       275
                           280
                                               285
Thr Tyr Arg Gln Ala Ile Thr Ser Ala Ala Ser Gly Cys Gln Ala Ala
                      295
                                           300
Leu Asp Ala Glu Arg Trp Leu Gly Ser Gln Asn Ile
                   310
<210> 260
<211> 316
<212> PRT
<213> Neisseria meningitidis
Met Ser Gln His Arg Lys Leu Ile Ile Leu Gly Ser Gly Pro Ala Gly
```

Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Asn Pro Val Ile 25 Ile Thr Gly Ile Ala Gln Gly Gly Gln Leu Met Thr Thr Glu Val 40 Asp Asn Trp Pro Ala Asp Ala Asp Gly Val Gln Gly Pro Glu Leu Met Ala Arg Phe Leu Ala His Ala Glu Arg Phe Gly Thr Glu Ile Ile Phe 70 75 Asp Gln Ile Asn Ala Val Asp Leu Gln Lys Arg Pro Phe Thr Leu Lys 90 Gly Asp Met Gly Glu Tyr Thr Cys Asp Ala Leu Ile Val Ala Thr Gly 105 Ala Ser Ala Lys Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe Ala Gly 115 120 125 Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn 135 140 Gln Asp Val Ala Val Val Gly Gly Asn Thr Ala Val Glu Glu Ala 150 155 Leu Tyr Leu Ala Asn Ile Ala Lys Thr Val Thr Leu Ile His Arg Arg 165 170 175 Ser Glu Phe Arg Ala Glu Lys Ile Met Ile Asp Lys Leu Met Lys Arg 180 185 Val Glu Glu Gly Lys Ile Ile Leu Lys Leu Glu Ser Asn Leu Gln Glu 200 Val Leu Gly Asp Asp Arg Gly Val Asn Gly Ala Leu Leu Lys Asn Asn 215 220 Asp Gly Ser Glu Gln Gln Ile Ala Val Ser Gly Ile Phe Ile Ala Ile 230 235 Gly His Lys Pro Asn Thr Asp Ile Phe Lys Gly Gln Leu Glu Met Asp 245 250 Glu Ala Gly Tyr Leu Lys Thr Lys Gly Gly Thr Ala Asp Asn Val Gly 265 Ala Thr Asn Ile Glu Gly Val Trp Ala Ala Gly Asp Val Lys Asp His 280 Thr Tyr Arg Gln Ala Ile Thr Ser Ala Ala Ser Gly Cys Gln Ala Ala 295 300 Leu Asp Ala Glu Arg Trp Leu Gly Ser Gln Asn Ile 310

<210> 261

<211> 316 <212> PRT

<213> Pseudomonas aeruginosa

<400> 261 Met Ser Glu Val Lys His Ser Arg Leu Ile Ile Leu Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Lys Pro 20 25 Val Val Ile Thr Gly Ile Gln Pro Gly Gly Gln Leu Thr Thr Thr Thr 40 45 Glu Val Asp Asn Trp Pro Gly Asp Val Glu Gly Leu Thr Gly Pro Ala Leu Met Thr Arg Met Gln Gln His Ala Glu Arg Phe Asp Thr Glu Ile 70 75 Val Tyr Asp His Ile His Thr Ala Glu Leu Gln Gln Arg Pro Phe Thr 85 90 Leu Lys Gly Asp Ser Gly Thr Tyr Thr Cys Asp Ala Leu Ile Ile Ala 100 105 Thr Gly Ala Ser Ala Gln Tyr Leu Gly Met Ser Ser Glu Glu Ala Phe 120 125 Met Gly Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 135 140 Arg Asn Gln Val Val Cys Val Val Gly Gly Asn Thr Ala Val Glu 150 155 Glu Ala Leu Tyr Leu Ala Asn Ile Ala Lys Glu Val His Leu Ile His

```
170
Arg Arg Asp Lys Leu Arg Ser Glu Lys Ile Leu Gln Asp Lys Leu Phe
                               185
           180
                                                   190
Asp Lys Ala Glu Asn Gly Asn Val His Leu His Trp Asn Thr Thr Leu
      195
                          200
Asp Glu Val Leu Gly Asp Ala Ser Gly Val Thr Gly Val Arg Leu Lys
                      215
                                          220
Ser Thr Ile Asp Gly Ser Thr Ser Glu Leu Ser Leu Ala Gly Val Phe
                                       235
Ile Ala Ile Gly His Lys Pro Asn Thr Asp Leu Phe Gln Gly Gln Leu
                                   250
               245
Glu Met Arg Asp Gly Tyr Leu Arg Ile His Gly Gly Ser Glu Gly Asn
           260
                               265
Ala Thr Gln Thr Ser Ile Glu Gly Val Phe Ala Ala Gly Asp Val Ala
                           280
                                               285
Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ala Gly Cys Met
                      295
                                         300
Ala Ala Leu Asp Ala Glu Lys Tyr Leu Asp Asp His
                   310
```

<210> 262

<211> 316

<212> PRT

<213> Pseudomonas aeruginosa

<400> 262 Met Pro Asp Thr Leu Arg His Ala Arg Val Ile Ile Leu Gly Ser Gly Pro Ala Gly Tyr Ser Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Lys 25 Pro Leu Leu Ile Thr Gly Met Gln Ala Gly Gly Gln Leu Thr Thr 35 40 Thr Glu Val Asp Asn Trp Pro Gly Asp Pro His Gly Leu Thr Gly Pro 55 Ala Leu Met Gln Arg Met Gln Glu His Ala Glu Arg Phe Glu Thr Glu 70 75 Ile Val Phe Asp His Ile His Ala Val Asp Leu Ala Gly Lys Pro Phe 90 85 Thr Leu Arg Gly Asp Asn Gly Thr Tyr Thr Cys Asp Ala Leu Ile Val 100 105 Ala Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Gln Ala 115 120 Phe Met Gly Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe 135 140 Tyr Arg Asn Arg Glu Val Ala Val Ile Gly Gly Asn Thr Ala Val 150 155 Glu Glu Ala Leu Tyr Leu Ala Asn Ile Ala Ser Arg Val Thr Leu Val 165 170 His Arg Arg Glu Thr Phe Arg Ala Glu Lys Ile Leu Gln Asp Lys Leu 185 Gln Ala Arg Val Ala Glu Gly Lys Ile Val Leu Lys Leu Asn Ala Glu 195 200 Val Asp Glu Val Leu Gly Asp Thr Met Gly Val Thr Gly Val Arg Leu 215 220 Lys Thr Arg Asp Gly Gly Ser Glu Glu Ile Ala Val Asp Gly Met Phe 230 235 Val Ala Ile Gly His Thr Pro Asn Thr Ser Leu Phe Glu Gly Gln Leu 245 250 Ala Leu Lys Asp Gly Tyr Leu Val Val Asn Gly Gly Arg Glu Gly Asn 260 265 Ala Thr Ala Thr Asn Val Pro Gly Val Phe Ala Ala Gly Asp Val Ala 280 285 Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ala Gly Cys Met 295 Ala Ala Leu Asp Val Glu Arg Tyr Leu Asp Ser Leu

```
<210> 263
<211> 345
<212> PRT
<213> Pyrococcus abyssi
<400> 263
Met Leu Leu Asn Ile His Gln Glu Ser Tyr Val Glu Val Val Lys Met
                                    10
Phe Ser Leu Gly Gly Leu Gly Lys Ser Arg Val Asp Glu Ser Lys Val
            20
                                25
Trp Asp Val Ile Ile Ile Gly Ala Gly Pro Ala Gly Tyr Thr Ala Ala
                            40
Ile Tyr Ala Ala Arg Phe Gly Leu Asp Thr Ile Ile Ile Thr Lys Asp
                        55
Leu Gly Gly Asn Met Ala Ile Thr Asp Leu Ile Glu Asn Tyr Pro Gly
                                       75
                    70
Phe Pro Glu Gly Ile Ser Gly Ser Glu Leu Ala Lys Arg Met Tyr Glu
               85
                                    90
His Val Lys Lys Tyr Gly Val Asp Val Ile Phe Asp Glu Val Val Arg
                                105
Ile Asp Pro Ala Glu Cys Ala Tyr Tyr Glu Gly Pro Cys Gln Phe Glu
                                                125
                           120
Val Lys Thr Ala Asn Gly Lys Glu Tyr Lys Gly Lys Thr Ile Ile Ile
  130
                        135
                                            140
Ala Val Gly Ala Glu Pro Arg Lys Leu His Val Pro Gly Glu Lys Glu
                    150
                                        155
Phe Thr Gly Arg Gly Val Ser Tyr Cys Ala Thr Cys Asp Gly Pro Leu
                                   170
                165
Phe Val Gly Lys Glu Val Ile Val Val Gly Gly Asn Thr Ala Leu
            180
                                185
                                                    190
Gln Glu Ala Leu Tyr Leu His Ser Ile Gly Val Lys Val Thr Leu Val
                            200
His Arg Arg Asp Lys Phe Arg Ala Asp Lys Ile Leu Gln Asp Arg Leu
                        215
                                            220
Lys Gln Ala Gly Ile Pro Thr Ile Leu Asn Thr Val Val Thr Glu Ile
                    230
                                        235
Arg Gly Thr Asn Lys Val Glu Ser Val Val Leu Lys Asn Val Lys Thr
                                   250
               245
Gly Glu Thr Phe Glu Lys Lys Val Asp Gly Val Phe Ile Phe Ile Gly
                               265
                                                    270
Tyr Glu Pro Lys Thr Asp Phe Val Lys His Leu Gly Ile Thr Asp Glu
                            280
Tyr Gly Tyr Ile Lys Val Asp Met Tyr Met Arg Thr Lys Val Pro Gly
                      295
                                            300
Ile Phe Ala Ala Gly Asp Ile Thr Asn Val Phe Lys Gln Ile Ala Val
                   310
                                       315
Ala Val Gly Gln Gly Ala Ile Ala Ala Asn Ser Ala Lys Glu Phe Ile
                325
                                   330
Glu Ser Trp Asn Gly Lys Ser Ile Glu
<210> 264
<211> 334
<212> PRT
<213> Rickettsia prowazekii
<400> 264
Met Tyr Asn Thr Asp Ile. Val Ile Ile Gly Ser Gly Pro Val Gly Leu
                                    10
Phe Ala Val Phe Gln Ala Gly Met Leu Gly Met Lys Cys His Val Ile
Asp Ala Gln Glu Val Ile Gly Gly Gln Cys Ile Thr Leu Tyr Pro Glu
                            40
```

Lys His Ile Tyr Asp Ile Pro Ala Tyr Pro Lys Ile Ala Ala Lys Glu

Leu Ile Lys Gln Leu Glu Ser Gln Ala Ala Pro Phe Asn Pro Val Tyr His Leu Asn Gln Gln Ala Thr Glu Leu Asn Lys His Asp Asp Phe Phe 85 90 Glu Ile Lys Thr Ser Lys Asn Thr Leu Ile Lys Ser Lys Val Ile Ile 100 105 Ile Ala Ala Gly Ala Gly Ala Phe Gly Pro Asn Lys Pro Pro Ile Ala 120 125 Asn Ile Glu Ala Phe Glu Gly Lys Ser Ile Phe Tyr Phe Ile Asn Asp 135 140 Lys Ser Lys Phe Leu Gly Lys Asn Ile Val Val Ala Gly Gly Gly Asp 150 155 Ser Ala Val Asp Trp Ala Ile Thr Leu Ser Glu Ile Ala Asn Lys Ile 165 170 Tyr Leu Val His Arg Arg Asp Lys Phe Thr Ala Ala Thr Glu Ser Val 180 185 Arg Gln Leu Arg His Ile Ala Glu Thr Gly Lys Ile Glu Leu Val Thr 195 200 205 Gly Tyr Gln Leu Asn Asn Leu Asp Gly His Asn Ser Glu Leu Arg Ser 215 Val Ile Val Lys Asp Leu Gln Asn Asn Ile Arg Lys Leu Asp Ala Asn 230 235 Ile Leu Leu Pro Phe Phe Gly Leu Lys Gln Asp Leu Gly Pro Leu Ala 245 250 Asn Trp Gly Phe Asn Val Arg Leu Gln His Ile Glu Val Asp Asn Tyr 260 265 Tyr Tyr Gln Thr Asn Ile Lys Gly Ile Tyr Ala Ile Gly Asp Val Ala 275 280 285 His Tyr Val Gly Lys Leu Lys Leu Ile Ile Thr Gly Phe Ala Glu Ala 295 300 Ala Cys Ser Leu His His Ala Tyr Ser Arg Val Phe Asp Gly Lys Ala 310 315 Leu His Phe Glu Tyr Ser Thr Asn Lys Tyr Glu Gln Lys Gln 325

<210> 265

<211> 311

<212> PRT

<213> Staphylococcus aureus

<400> 265

Met Thr Glu Ile Asp Phe Asp Ile Ala Ile Ile Gly Ala Gly Pro Ala · 10 Gly Met Thr Ala Ala Val Tyr Ala Ser Arg Ala Asn Leu Lys Thr Val 20 25 Met Ile Glu Arg Gly Ile Pro Gly Gly Gln Met Ala Asn Thr Glu Glu 35 40 Val Glu Asn Phe Pro Gly Phe Glu Met Ile Thr Gly Pro Asp Leu Ser 55 60 Thr Lys Met Phe Glu His Ala Lys Lys Phe Gly Ala Val Tyr Gln Tyr 70 75 Gly Asp Ile Lys Ser Val Glu Asp Lys Gly Glu Tyr Lys Val Ile Asn 85 90 Phe Gly Asn Lys Glu Leu Thr Ala Lys Ala Val Ile Ile Ala Thr Gly 100 105 Ala Gly Tyr Lys Lys Ile Gly Val Pro Gly Glu Gln Glu Leu Gly Gly 115 120 125 Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Lys Asn 135 140 Lys Arg Leu Phe Val Ile Gly Gly Gly Asp Ser Ala Val Glu Glu Gly 150 155 Thr Phe Leu Thr Lys Phe Ala Asp Lys Val Thr Ile Val His Arg Arg 170 1.65 175 Asp Glu Leu Arg Ala Gln Arg Ile Leu Gln Asp Arg Ala Phe Lys Asn 180 185 Asp Lys Ile Asp Phe Ile Trp Ser His Thr Leu Lys Ser Ile Asn Glu

```
195
                           200
                                               205
Lys Asp Gly Lys Val Gly Ser Val Thr Leu Thr Ser Thr Lys Asp Gly
                       215
                                           220
Ser Glu Glu Thr His Glu Ala Asp Gly Val Phe Ile Tyr Ile Gly Met
                   230
                                     235
Lys Pro Leu Thr Ala Pro Phe Lys Asp Leu Gly Ile Thr Asn Asp Val
                                   250
Gly Tyr Ile Val Thr Lys Asp Asp Met Thr Thr Ser Val Pro Gly Ile
           260
                               265
Phe Ala Ala Gly Asp Val Arg Asp Lys Gly Leu Arg Gln Ile Val Thr
       275
                          280
Ala Thr Gly Asp Gly Ser Ile Ala Ala Gln Ser Thr Ser Gly Tyr Ile
                      295
Glu His Leu Asn Asp Gln Ala
                  310
```

<210> 266 <211> 326 <212> PRT <213> Streptomyces coelicolor

Glu Val Val Ala Val Ala

325

<400> 266 Met Ser Thr Ala Lys Asp Val Arg Asp Val Ile Val Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Thr Ala Arg Ala Ser Leu Asn Pro Leu Val Phe Gly Gly Ala Ile Phe Val Gly Gly Ser Leu Thr Thr 40 Thr Thr Glu Val Glu Asn Phe Pro Gly Phe Pro Asp Gly Val Gln Gly 55 Pro Glu Leu Met Glu Asn Met Arg Ala Gln Ala Glu Arg Phe Gly Ala Glu Met Val Asp Asp Asp Ile Val Ala Val Asp Leu Thr Gly Asp Val 85 90 95 Lys Thr Val Thr Asp Thr Ala Gly Thr Val His Arg Ala Arg Thr Val 100 105 110 Ile Val Ala Thr Gly Ser Gly Tyr Arg Lys Leu Gly Val Pro Lys Glu 120 Asp Glu Leu Ser Gly Arg Gly Val Ser Trp Cys Ala Thr Cys Asp Gly 135 Phe Phe Arg Asp Arg Asp Ile Val Val Gly Gly Asp Thr 150 155 Ala Met Glu Glu Ala Thr Phe Leu Thr Arg Phe Ala Arg Ser Val Thr . 165 170 Val Val His Arg Arg Ser Ala Leu Arg Ala Ser Gln Val Met Gln Asn 180 185 190 Arg Ala Phe Ser Glu Asp Lys Ile Ser Leu Ala Phe Asp Ser Glu Val 200 205 Ala Thr Leu His Glu Glu Asn Gly Met Leu Ser Gly Met Thr Leu Arg 215 220 Asp Thr Leu Thr Gly Glu Thr Arg Glu Leu Ala Thr Thr Gly Leu Phe 230 235 Ile Ala Ile Gly His Asp Pro Arg Thr Glu Leu Phe Lys Gly Gln Leu 245 250 His Leu Asp Ser Glu Gly Tyr Leu Met Val Glu Ser Pro Ser Thr Arg 265 260 Thr Asn Val Pro Gly Val Phe Gly Ala Gly Asp Val Val Asp His Thr 275 280 285 Tyr Arg Gln Ala Ile Thr Ala Ala Ser Ser Gly Cys Ala Ala Ala Leu 295 300 Asp Ala Glu Arg Tyr Leu Ala Ala Arg Ser Asp Thr Ser Val Ser Ala 310 315

-158-

<210> 267

<211> 558 <212> PRT <213> Streptomyces coelicolor <400> 267 Met Ala Gln Ala Asp Gly Glu Thr Arg Thr Val Ile Met Thr Val Asp 10 Asp Asp Pro Gly Val Ser Arg Ala Val Ala Arg Asp Leu Arg Arg Arg 20 25 Tyr Gly Ala Thr Tyr Arg Ile Val Arg Ala Glu Ser Gly Glu Ser Ala Leu Asp Ala Leu Arg Glu Leu Lys Leu Arg Gly Asp Leu Val Ala Val 55 Ile Leu Ala Asp Tyr Arg Met Pro Gln Met Asn Gly Ile Glu Phe Leu 70 Glu Gln Ala Leu Asp Val Tyr Pro Gly Ala Arg Arg Val Leu Leu Thr 90 Ala Tyr Ala Asp Thr Asn Ala Ala Ile Asp Ala Ile Asn Val Val Asp 100 105 Leu Asp His Tyr Leu Leu Lys Pro Trp Asp Pro Pro Glu Glu Lys Leu 120 125 115 Tyr Pro Val Leu Asp Asp Leu Leu Gln Ala Trp Arg Ala Gly Asp His 135 140 Arg Pro Val Pro Ser Thr Lys Val Val Gly His Arg Trp Ser Ala Arg 150 155 Ser Ser Glu Val Arg Glu Phe Leu Ala Arg Asn Gln Val Pro Tyr Arg 170 165 Trp Tyr Ser Ser Asp Glu Pro Glu Gly Arg Arg Leu Leu Ser Ala Ala 180 185 190 Gly Gln Asp Gly Gln Arg Leu Pro Val Val Ile Thr Pro Asp Gly Thr 195 200 205 Pro Leu Val Glu Pro Glu Ala Pro Glu Leu Ala Ala Arg Val Gly Leu 215 · 220 Ala Thr Thr Pro Thr Ser Asp Phe Tyr Asp Leu Val Val Ile Gly Gly 235 230 Gly Pro Ala Gly Leu Gly Ala Ala Val Tyr Gly Ala Ser Glu Gly Leu 245 250 Arg Thr Val Leu Val Glu Arg Ser Ala Thr Gly Gly Gln Ala Gly Gln . 265 Ser Ser Arg Ile Glu Asn Tyr Leu Gly Phe Pro Asp Gly Val Ser Gly 280 285 Gly Gln Leu Thr Glu Arg Ala Arg Gln Ala Ala Arg Phe Gly Ala 295 300 Glu Ile Leu Thr Ala Arg Glu Val Thr Gly Leu Glu Ala Asn Gly Ala 310 315 Ala Arg Val Val Arg Phe Ser Asp Gly Ser Ala Ile Ala Ala His Ser 325 330 335 Val Ile Leu Ala Thr Gly Val Ser Tyr Arg Gln Leu Thr Ala Pro Gly 345 340 350 Thr Glu Asp Leu Ala Gly Cys Gly Val Phe Tyr Gly Ser Ala Leu Thr 365 360 Glu Ala Ala Ser Cys Gln Gly His Asp Val Tyr Ile Val Gly Gly Ala 375 380 Asn Ser Ala Gly Gln Ala Ala Met Tyr Leu Ala Arg Gly Ala Lys Ser 395 Val Thr Leu Leu Val Arg Gly Gly Ser Leu Glu Ala Ser Met Ser Tyr 405 410 Tyr Leu Ile Gln Gln Ile Glu Glu Thr Pro Asn Ile Arg Val Arg Cys 420 425 430 Gly Thr Leu Val Glu Gly Ala His Gly Asp Gly His Leu Glu Arg Leu 440 Thr Leu Arg Asp Ala Ala Ser Gly Ala Thr Glu Leu Val Asp Ala Gln 455 Trp Leu Phe Val Phe Ile Gly Ala Ala Pro Leu Thr Asp Trp Leu Asp 470 475 Gly Thr Val Leu Arg Asp Glu Arg Gly Phe Ile Leu Ala Gly Pro Asp

```
490
                485
Leu Thr Pro Asp Gly Arg Pro Pro Ala Gly Trp Glu Leu Asp Arg Pro
                                505
                                                    510
Pro Tyr His Leu Glu Thr Ser Val Pro Gly Val Phe Val Ala Gly Asp
                        520
      515
Ala Arg Ala Glu Ser Ala Lys Arg Val Ala Ser Ala Val Gly Glu Gly
                    535
Ala Met Ala Val Met Leu Val His Arg Tyr Leu Glu Gln Ser
                    550
<210> 268
<211> 303
<212> PRT
<213> Streptococcus pneumoniae
<400> 268
Met Tyr Asp Thr Ile Ile Ile Gly Ala Gly Pro Ala Gly Met Thr Ala
                                    10
Ala Leu Tyr Ala Ala Arg Ser Asn Leu Lys Val Ala Leu Ile Glu Gly
                                25
Gly Leu Pro Gly Gly Gln Met Asn Asn Thr Ser Asp Ile Glu Asn Tyr
Pro Gly Tyr Ala Asn Ile Ser Gly Pro Glu Leu Ala Glu Lys Met Phe
                        55
Glu Pro Leu Glu Asn Leu Gly Val Glu His Ile Tyr Gly Tyr Val Glu
                   70
                                       75
Asn Val Glu Asp His Gly Asp Phe Lys Lys Val Met Thr Asp Asp Gln
                                   90
Thr Tyr Glu Thr Arg Thr Val Ile Val Ala Thr Gly Ser Lys His Arg
                                105
Pro Leu Gly Val Pro Gly Glu Glu Leu Asn Ser Arg Gly Val Ser
        115
                                               125
                           120
Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Arg Asp Gln Asp Leu Leu
                        135
                                           140
Val Val Gly Gly Gly Asp Ser Ala Val Glu Glu Ala Leu Phe Leu Thr
                   150
                                       155
Arg Phe Ala Lys Thr Val Thr Ile Val His Arg Arg Asp Gln Leu Arg
                                   170
               165
Ala Gln Lys Val Leu Gln Asp Arg Ala Phe Ala Asn Glu Lys Ile Ser
                               1.85
                                                   190
Phe Ile Trp Asp Ser Val Val Arg Glu Ile Lys Gly Glu Asn Arg Val
                                                205
       195
                           200
Glu Ser Val Val Phe Glu Asn Val Lys Thr Gly Gln Val Thr Glu Gln
                       215
                                           220
Ala Phe Gly Gly Val Phe Ile Tyr Val Gly Leu Asp Pro Leu Ser Asp
                   230
                                       235
Phe Val Lys Glu Leu Asn Ile Gln Asp Gln Ala Gly Trp Ile Val Thr
               245
                                   250
Asp Asn His Met Lys Thr Ala Val Asp Gly Ile Phe Ala Val Gly Asp
                               265
Val Arg Leu Lys Asp Leu Arg Gln Val Thr Thr Ala Val Gly Asp Gly
                            280
Ala Ile Ala Gly Gln Glu Ala Tyr Lys Phe Ile Thr Glu His Ser
                        295
<210> 269
<211> 330
<212> PRT
<213> Streptococcus pyogenes
<400> 269
Met Lys Asp Lys Ala Tyr Asp Ile Thr Ile Ile Gly Gly Pro Ile
                                    10
Gly Leu Phe Ala Ala Phe Tyr Ala Gly Leu Arg Gly Val Thr Val Lys
           20
```

```
Ile Ile Glu Ser Leu Ser Glu Leu Gly Gly Gln Pro Ala Ile Leu Tyr
Pro Glu Lys Met Ile Tyr Asp Ile Pro Ala Tyr Pro Ser Leu Thr Gly
Val Glu Leu Thr Glu Asn Leu Ile Lys Gln Leu Ser Arg Phe Glu Asp
                    70
                                        75
Arg Thr Thr Ile Cys Leu Lys Glu Glu Val Leu Thr Phe Asp Lys Val
                85
Lys Gly Gly Phe Ser Ile Arg Thr Asn Lys Ala Glu His Phe Ser Lys
                               105
Ala Ile Ile Ile Ala Cys Gly Asn Gly Ala Phe Ala Pro Arg Thr Leu
                           120
       115
                                               125
Gly Leu Glu Ser Glu Glu Asn Phe Ala Asp His Asn Leu Phe Tyr Asn
                        135
                                            140
Val His Gln Leu Asp Gln Phe Ala Gly Gln Lys Val Val Ile Cys Gly
                  150
                                      155
Gly Gly Asp Ser Ala Val Asp Trp Ala Leu Ala Leu Glu Asp Ile Ala
                                   170
               165
                                                       175
Glu Ser Val Thr Val Val His Arg Arg Asp Ala Phe Arg Ala His Glu
           180
                                185
His Ser Val Glu Leu Leu Lys Ala Ser Thr Val Asn Leu Leu Thr Pro
                           200
Tyr Val Pro Lys Ala Leu Lys Gly Ile Gly Asn Leu Ala Glu Lys Leu
                       215
                                            220
Val Ile Gln Lys Val Lys Glu Asp Glu Val Leu Glu Leu Glu Leu Asp
                   230
                                       235
Ser Leu Ile Val Ser Phe Gly Phe Ser Thr Ser Asn Lys Asn Leu Lys
               245
                                   250
Asn Trp Asn Leu Asp Tyr Lys Arg Ser Ser Ile Thr Val Ser Pro Leu
                                265
Phe Gln Thr Ser Gln Glu Gly Ile Phe Ala Ile Gly Asp Ala Ala Ala
                            280
                                               285
Tyr Asn Gly Lys Val Asp Leu Ile Ala Thr Gly Phe Gly Glu Ala Pro
                       295
                                           300
Thr Ala Val Asn Gln Ala Ile Asn Tyr Ile Tyr Pro Asp Arg Asp Asn
                    310
Arg Val Val His Ser Thr Ser Leu Ile Asp
```

<210> 270

<211> 325

<212> PRT

<213> Sulfolobus solfataricus

<400> 270 Met Pro Leu Lys Thr Tyr Asp Thr Ile Ile Val Gly Ala Gly Ile Ala 10 Gly Leu Ser Ala Ala Leu Tyr Ser Ser Arg Gln Lys Leu Ser Thr Leu 20 25 Val Leu Ser Lys Asp Leu Gly Gly Gln Leu Thr Leu Thr Asp Leu Ile Glu Asn Tyr Pro Gly Ile Glu Ser Thr Gly Gly Leu Thr Leu Ala Gln 55 Lys Ile Glu Lys Gln Ala Lys Lys Phe Gly Ala Glu Phe Ile Tyr Gly 75 70 Glu Glu Val Lys Glu Ile Ala Gln Glu Ser Asp Leu Phe Ile Ile Lys 90 Gly Ile Lys Gly Glu Tyr Ala Gly Arg Ala Leu Ile Leu Ala Phe Gly 105 Lys Thr Pro Arg Glu Ile Asn Val Pro Gly Glu Glu Glu Phe Lys Gly 120 125 Lys Gly Val Ser Tyr Cys Ala Ile Cys Asp Ala Ala Phe Phe Lys Gly 135 Lys Pro Ala Ala Val Ile Gly Glu Gly Glu Pro Gly Ile Glu Ala Ile 150 155 Glu Leu Leu Ser Asn Tyr Ala Asn Pro Ala Tyr Tyr Ile Thr Ser Ser

```
165
                                   170
Ser Tyr Leu Ala Gly Glu Glu Glu Ile Val Lys Asn Val Val Asn Lys
                              185
Pro Thr Val Lys Ile Leu Thr Ser Ser Arg Val Leu Glu Ile Arg Gly
                          200
                                               205
Asn Ser Lys Val Glu Glu Leu Val Ile Lys Arg Gly Asp Glu Ile Leu
                                           220
                       215
Gln Leu Lys Val Asp Gly Val Ile Ile Glu Met Gly Tyr Thr Leu Lys
                   230
                                       235
Thr Glu Phe Leu Lys Gly Phe Val Glu Leu Asn Glu Lys Gly Glu Ile
               245
                                   250
Ile Val Asp Glu Leu Gly Arg Thr Ser Arg Glu Gly Val Phe Ala Ala
           260
                               265
Gly Asp Val Thr Gln Thr Pro Tyr Lys Gln Ala Val Val Ala Ala Ala
                        280
       275
Glu Gly Val Lys Ala Ala Leu Ser Ala Tyr Asn Tyr Ile Arg Ser Lys
                      295 '
                                          300
Arg Gly Leu Pro Pro Val Thr Val Asp Trp Lys Ala Glu Lys Lys
                                       315
Val Ser Phe Arg Leu
```

<210> 271

<211> 323

<212> PRT

<213> Sulfolobus solfataricus

<400> 271 Met Ser Leu Leu Pro Arg Thr Thr Ser Val Lys Pro Gly Glu Lys Phe Asp Val Ile Ile Val Gly Leu Gly Pro Ala Ala Tyr Gly Ala Ala Leu Tyr Ser Ala Arg Tyr Met Leu Lys Thr Leu Val Ile Gly Glu Thr Pro 35 40 Gly Gly Gln Leu Thr Glu Ala Gly Ile Val Asp Asp Tyr Leu Gly Leu 55 60 Ile Glu Ile Gln Ala Ser Asp Met Ile Lys Val Phe Asn Lys His Ile 70 75 Glu Lys Tyr Glu Val Pro Val Leu Leu Asp Ile Val Glu Lys Ile Glu 85 Asn Arg Gly Asp Glu Phe Val Val Lys Thr Lys Arg Lys Gly Glu Phe 105 100 Lys Ala Asp Ser Val Ile Leu Gly Ile Gly Val Lys Arg Arg Lys Leu 125 120 Gly Val Pro Gly Glu Gln Glu Phe Ala Gly Arg Gly Ile Ser Tyr Cys 140 135 Ser Val Cys Asp Ala Pro Leu Phe Lys Asn Arg Val Val Ala Val Ile 155 150 Gly Gly Gly Asp Ser Ala Leu Glu Gly Ala Glu Ile Leu Ser Ser Tyr 170 165 Ser Thr Lys Val Tyr Leu Ile His Arg Arg Asp Thr Phe Lys Ala Gln 190 185 Pro Ile Tyr Val Glu Thr Val Lys Lys Pro Asn Val Glu Phe Val 200 205 Leu Asn Ser Val Val Lys Glu Ile Lys Gly Asp Lys Val Val Lys Gln 215 220 Val Val Val Glu Asn Leu Lys Thr Gly Glu Ile Lys Glu Leu Asn Val 230 235 Asn Gly Val Phe Ile Glu Ile Gly Phe Asp Pro Pro Thr Asp Phe Ala 250 245 Lys Ser Asn Gly Ile Glu Thr Asp Thr Asn Gly Tyr Ile Lys Val Asp 265 260 Glu Trp Met Arg Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Cys 280 285 275 Thr Ser Ala Trp Leu Gly Phe Arg Gln Val Ile Thr Ala Val Ala Gln

Gly Ala Val Ala Ala Thr Ser Ala Tyr Arg Tyr Val Thr Glu Lys Lys 305 310 315 320 Gly Lys Lys

<210> 272 <211> 332 <212> PRT <213> Sulfolobus solfataricus <400> 272 Met Asp Glu Tyr Asp Ile Val Val Ile Gly Gly Gly Pro Val Gly Leu Phe Gly Thr Phe Tyr Ala Gly Leu Arg Asp Met Lys Thr Leu Leu Ile Asp Ala Gln Asp Glu Leu Gly Gly Gln Leu Val Ser Leu Tyr Pro Glu 40 Lys Ile Val Tyr Asp Val Gly Gly Leu Ala Gly Ile Gln Ala Tyr Glu 55 Leu Ala Gln Arg Leu Ile Glu Gln Ala Lys Met Phe Gly Pro Asp Ile 70 Lys Val Asn Glu Leu Ala Asp Met Ile Glu Lys Thr Asn Asp Asn Met 85 90 Trp Ile Val Lys Thr Asp Lys Ala Thr Tyr Lys Thr Lys Thr Ile Phe 105 Ile Ala Ala Gly Ile Gly Lys Ile Val Pro Ser Arg Leu Gly Ala Lys 115 120 125 Gly Glu Ile Glu Tyr Glu Asn Arg Gly Val Tyr Tyr Thr Val Arg Arg 135 140 Lys Lys Asp Phe Glu Gly Lys Arg Val Leu Ile Val Gly Gly Gly Asp 150 155 Ser Ala Val Asp Trp Ala Leu Thr Leu Ala Pro Val Ala Lys Ser Val 170 165 Thr Leu Ile His Arg Arg Asp Gln Phe Arg Ala His Glu Arg Ser Val 185 190 180 Lys Glu Leu Phe Arg Val Ala Asn Val Tyr Val Trp His Glu Leu Lys 195 200 205 Glu Val Lys Gly Asp Gly Asn Lys Val Thr Gln Ala Ile Ile Phe Asp 215 Asn Arg Thr Lys Glu Glu Lys Val Leu Asp Val Asp Ser Val Ile Ile 235 230 Ser Ile Gly Tyr Lys Gly Asp Leu Gly Asn Ile Pro Lys Trp Gly Val 245 250 255 Thr Met Lys Gly Arg Asp Ile Val Val Asn Gly Arg Met Glu Thr Asn 260 265 270 Leu Pro Gly Val Tyr Ala Gly Gly Asp Ile Val Gln Met Glu Gly Ser 275 280 Pro Lys Leu Ala Leu Ile Ala Val Gly Phe Ala His Ala Ala Ile Ala 295 300 Ile Ser Val Ala Lys Lys Tyr Val Glu Pro Asn Ala Ser Leu Phe Ala 310 315 Gly His Ser Ser Glu Met Asp Lys Phe Lys Pro Lys 325 330

<210> 273 <211> 324

<212> PRT

<213> Rhizobium loti

<400> 273

Met Thr Thr Lys His Ala Pro Val Leu Ile Ile Gly Ser Gly Pro Ala

1 5 10 15

Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Met Leu Lys Pro Met
20 25 30

Leu Val Ala Gly Leu Gln Gln Gly Gly Gln Leu Met Ile Thr Thr Asp

```
40
Val Glu Asn Tyr Pro Gly Phe Ala Asp Pro Ile Gln Gly Pro Trp Leu
Met Glu Gln Met Met Lys Gln Ala Glu His Val Gly Thr Asp Ile Ile
Asn Asp Ile Ile Thr Glu Val Asp Leu Asn Val Arg Pro Phe Arg Ala
                85
                                    90
Lys Gly Asp Ser Gly Thr Thr Tyr Thr Ala Asp Ala Leu Ile Ile Ala
                                105
Thr Gly Ala Gln Ala Lys Trp Leu Gly Ile Pro Thr Glu Gln Asp Phe
                            120
Met Gly Phe Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr
                       135
                                            140
Arg Gly Lys Asp Val Ala Val Val Gly Gly Asn Ser Ala Val Glu
                    150
                                        155
Glu Ala Leu Tyr Leu Ser Asn Leu Ala Lys Ser Val Thr Val Ile His
               165
                                   170
Arg Arg Ser Asp Phe Arg Ala Glu Arg Ile Leu Arg Glu Arg Leu Leu
           180
                                185
Gln Lys Asp Asn Val Arg Val Ile Trp Asp Thr Val Val Asp Glu Ile
                            200
Thr Gly Arg Pro Gly Lys Ala Pro Leu Pro Pro Ser Val Glu Gly Leu
                       215
Lys Leu Lys His Ala Val Thr Gly Ala Glu Thr His Leu Lys Val Asp
                    230
                                        235
Gly Val Phe Val Ala Ile Gly His Ala Pro Ala Val Glu Leu Phe Val
               245
                                    250
Gly Lys Leu Lys Gln Lys Pro Asn Gly Tyr Leu Trp Thr Ala Pro Asn
                               265
Ser Thr Arg Thr Asp Val Pro Gly Val Phe Ala Ala Gly Asp Val Thr
       275
                           280
Asp Asp Val Tyr Arg Gln Ala Val Thr Ala Ala Gly Leu Gly Cys Met
                       295
                                           300
Ala Ala Leu Glu Ala Glu Lys Tyr Leu Ala Gly Ile Glu Val His Arg
Glu Ala Ala Glu
```

<210> 274 <211> 343 <212> PRT <213> Rhizobium loti

<400> 274 Met Thr Gly Ile Ile Ser Thr Asp Val Leu Ile Val Gly Ala Gly Pro 10 Val Gly Leu Phe Ala Val Phe Glu Leu Gly Leu Phe Asp Met Lys Cys His Leu Ile Asp Ile Leu Asp Lys Pro Gly Gly Gln Cys Ala Glu Leu Tyr Pro Glu Lys Pro Ile Tyr Asp Ile Pro Gly Trp Pro Ser Ile Ser 55 Ala Gln Gly Leu Val Asp Lys Leu Leu Glu Gln Ile His Pro Phe Lys 70 75 Pro Asp Phe Thr Tyr Asn Arg Met Val Ser Ser Leu Glu Lys Leu Glu 85 90 Asp Gly Ser Phe Arg Val Thr Thr Asp Glu Asn Glu Val Phe Glu Ala Lys Val Val Ile Ala Ala Gly Gly Gly Ser Phe Gln Pro Lys Arg 120 125 Pro Pro Ile Pro Gly Ile Glu Pro Tyr Glu Gly Lys Ser Val Phe Tyr 135 140 Ser Val Arg Arg Met Glu Asp Phe Arg Gly His Asp Leu Val Ile Val 150 155 Gly Gly Gly Asp Ser Ala Leu Asp Trp Thr Leu Asn Leu Gln Pro Val

170

```
Ala Lys Ser Val Thr Leu Val His Arg Arg Pro Glu Phe Arg Ala Ala
                                185
            180
Pro Asp Ser Val Asn Lys Met Tyr Ala Met Gln Glu Met Lys Gln Leu
                            200
        195
Glu Phe Arg Val Gly Gln Val Thr Gly Leu Thr Gly Ala Asp Gly Gln
                        215
                                            220
Leu Ser Ser Ala Thr Ile Lys Gly Gly Pro Asp Gly Asp Ile Glu Val
                    230
                                        235
Pro Cys Thr Arg Met Leu Pro Phe Phe Gly Leu Thr Met Lys Leu Gly
                245
                                    250
Pro Ile Ala Glu Trp Gly Leu Asn Leu His Glu Asn Leu Ile Pro Val
            260
                                265
                                                    270
Asp Thr Glu Lys Phe Gln Thr Ser Val Pro Gly Ile Phe Ala Val Gly
                            280
Asp Ile Asn Ser Tyr Pro Gly Lys Leu Lys Leu Ile Leu Ser Gly Phe
                       295
                                           300
 290
His Glu Val Ala Leu Met Ala Gln Ala Ala Lys Arg Ile Val Ser Pro
                    310
                                       315
Gly Glu Arg Ile Val Phe Gln Tyr Thr Thr Ser Ser Thr Ser Leu Gln
                325
Lys Lys Leu Gly Val Val Gly
            340
<210> 275
<211> 15
<212> PRT
<213> Saccharomyces cerevisiae
<220>
<221> VARIANT
<222> 9, 11
<223> Xaa = Any Amino Acid
<400> 275
Val His Asn Ile Val Thr Ile Ile Xaa Ser Xaa Pro Ala Ala His
<210> 276
<211> 104
<212> PRT
<213> Staphylococcus aureus
<400> 276
Met Ala Ile Val Lys Val Thr Asp Ala Asp Phe Asp Ser Lys Val Glu
                                    10
Ser Gly Val Gln Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys
                                25
Lys Met Ile Ala Pro Val Leu Glu Glu Leu Ala Ala Asp Tyr Glu Gly
                            40
Lys Ala Asp Ile Leu Lys Leu Asp Val Asp Glu Asn Pro Ser Thr Ala
                        55
Ala Lys Tyr Glu Val Met Ser Ile Pro Thr Leu Ile Val Phe Lys Asp
                                        75
                    70
Gly Gln Pro Val Asp Lys Val Val Gly Phe Gln Pro Lys Glu Asn Leu
                                    90
                85
Ala Glu Val Leu Asp Lys His Leu
            100
<210> 277
<211> 92
<212> PRT
<213> Staphylococcus xylosus
<400> 277
```

 Met Ala Glu Gln Val Asp Phe Asp Ile Ala Ile Ile Gly Ala Gly Pro 1
 5
 10
 10
 16
 15
 15

 Ala Gly Met Thr Ala Ala Val Tyr Ala Ser Arg Ala Asn Leu Ser Thr 20
 25
 25
 30
 30
 77
 16
 16
 16
 16
 16
 17
 17
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 18
 <t

<210> 278 <211> 319 <212> PRT <213> Thermoplasma acidophilum

<400> 278 Met Glu Phe Asn Leu His Ala Val Ser Ser Glu Glu Lys Glu Arg Asp 1 1.0 Phe Asp Val Val Ile Val Gly Ala Gly Ala Ala Gly Phe Ser Ala Ala 25 Val Tyr Ala Ala Arg Ser Gly Phe Ser Val Ala Ile Leu Asp Lys Ala 40 45 Val Ala Gly Gly Leu Thr Ala Glu Ala Pro Leu Val Glu Asn Tyr Leu 55 Gly Phe Lys Ser Ile Val Gly Ser Glu Leu Ala Lys Leu Phe Ala Asp 70 75 His Ala Ala Asn Tyr Ala Lys Ile Arg Glu Gly Val Glu Val Arg Ser 85 Ile Lys Lys Thr Gln Gly Gly Phe Asp Ile Glu Thr Asn Asp Asp Thr 105 110 Tyr His Ala Lys Tyr Val Ile Ile Thr Thr Gly Thr Thr His Lys His

Leu Gly Val Lys Gly Glu Ser Glu Tyr Phe Gly Lys Gly Thr Ser Tyr

120

135

125

140

Leu Lys Asp Ser Gly Val Lys Leu Asp Glu Arg Gly Tyr Ile Val Val 260 265 270

Asp Ser Arg Gln Arg Thr Ser Val Pro Gly Val Tyr Ala Ala Gly Asp

275 280 285 Val Thr Ser Gly Asn Phe Ala Gln Ile Ala Ser Ala Val Gly Asp Gly

290 295 300 . Cys Lys Ala Ala Leu Ser Leu Tyr Ser Asp Ser Ile Ser Lys Lys 305 310 315

<210> 279 <211> 317 <212> PRT <213> Thermotoga maritima

115

130

```
<400> 279
Met Val Phe Phe Asp Thr Gly Ser Leu Lys Lys Lys Glu Ile Lys Asp
Lys Tyr Asp Ile Val Val Val Gly Gly Pro Ala Gly Leu Thr Ser
Ala Ile Tyr Ala Arg Arg Ala Gly Leu Ser Val Leu Val Val Glu Lys
        35
                            40
Ala Ile Glu Gly Gly Tyr Val Asn Leu Thr His Leu Val Glu Asn Tyr
                        55
Pro Gly Phe Pro Ala Ile Ser Gly Glu Glu Leu Ala Ser Lys Phe Lys
                    70
                                        75
Glu His Ala Glu Lys Phe Gly Ala Asp Ile Tyr Asn Ala Glu Val Val
                85
                                    90
Lys Leu Glu Val Gln Gly Asp Lys Lys Val Val Glu Leu Asp Asp Gly
            100
                                105
                                                    110
Lys Arg Ile Glu Ala Pro Val Val Ile Val Ala Thr Gly Ala Asn Pro
                            120
Lys Lys Leu Asn Val Pro Gly Glu Lys Glu Phe Phe Gly Lys Gly Val
    130
                        135
                                            140
Ser Tyr Cys Ala Thr Cys Asp Gly Tyr Leu Phe Ala Gly Lys Asp Val
                    150
                                        155
Ile Val Val Gly Gly Asp Ser Ala Cys Asp Glu Ser Ile Phe Leu
                                                        175
                165
                                    170
Ser Asn Ile Val Asn Lys Ile Thr Met Ile Gln Leu Leu Glu Thr Leu
            180
                                185
Thr Ala Ala Lys Val Leu Gln Glu Arg Val Leu Asn Asn Pro Lys Ile
        195
                            200
Glu Val Ile Tyr Asn Ser Thr Val Arg Glu Ile Arg Gly Lys Asp Lys
                        215
                                            220
Val Glu Glu Val Val Ile Glu Asn Val Lys Thr Gly Glu Thr Lys Val
                    230
                                        235
Leu Lys Ala Asp Gly Val Phe Ile Phe Ile Gly Leu Asp Pro Asn Ser
                245
                                    250
Lys Leu Leu Glu Gly Leu Val Glu Leu Asp Pro Tyr Gly Tyr Val Ile
                                265
                                                    270
Thr Asp Glu Asn Met Glu Thr Ser Val Lys Gly Ile Tyr Ala Val Gly
                            280
                                                285
Asp Val Arg Lys Lys Asn Leu Arg Gln Ile Val Thr Ala Val Ala Asp
                       295
                                            300
Gly Ala Ile Ala Val Glu His Ala Ala Lys His Tyr Phe
                    310
```

<400> 280 Met Asn Leu Tyr Arg Gly Met Glu Phe Asn Leu Arg Ser Val Ser Thr 10 Glu Ala Lys Glu Arg Asp Phe Asp Val Ile Ile Ile Gly Ala Gly Ala 20 25 Ala Gly Phe Ser Ala Ala Val Tyr Ala Ser Arg Ser Gly Leu Ser Ala 35 40 Val Ile Leu Asp Lys Asn Val Ala Gly Gly Leu Thr Ala Glu Ala Pro Leu Val Glu Asn Tyr Leu Gly Phe Lys Ser Ile Val Gly Ser Asp Leu 70 75 Ala Lys Asn Phe Ala Glu His Ala Ser Glu Tyr Ala Ser Ile Arg Glu 90 Gly Val Glu Val Lys Ser Val Lys Lys Gly Asp Gly Gly Phe Ile Val 105 110 Asp Thr Ser Asp Gly Glu Tyr His Ser Lys Tyr Ile Ile Ile Thr Thr 120 125 Gly Thr Thr His Lys His Leu Gly Val Lys Gly Glu Ala Glu Tyr Phe 135 140

<sup>&</sup>lt;210> 280

<sup>&</sup>lt;211> 326

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Thermoplasma volcanium

```
Gly Lys Gly Val Ser Tyr Cys Ser Thr Cys Asp Gly Tyr Leu Phe Lys
                    150
                                        155
Asn Lys Asn Val Val Thr Ile Gly Gly Gly Asn Ser Gly Ala Ile Ala
                165
                                    170
Ala Ile Ser Met Ser Glu Tyr Val Lys Asn Ala Thr Ile Val Glu Tyr
            180
                                185
                                                    190
Met Pro Arg Tyr Met Cys Glu Asn Ala Tyr Ile Glu Glu Ile Lys Lys
       195
                            200
                                                205
Arg Lys Ile Pro Tyr Ile Met Asn Ala Gln Val Thr Glu Ile Val Gly
   210
                        215
                                            220
Asp Gly Lys Lys Val, Thr Gly Val Lys Tyr Lys Asp Arg Ser Ser Gly
                                        235
                    230
                                                            240
Glu Glu Lys Thr Leu Pro Ala Asp Gly Val Phe Val Tyr Val Gly Leu
                245
                                    250
                                                        255
Ile Pro Gln Thr Ser Phe Leu Lys Asp Ser Gly Val Lys Leu Asp Glu
            260 .
                                265
Arg Gly Tyr Ile Ile Val Asp Gly Arg Gln Arg Thr Asn Val Pro Gly
       275
                            280
Ile Tyr Ala Ala Gly Asp Val Thr Ser Gly Ser Phe Ala Gln Ile Ala
   290
                        295
                                            300
Ser Ala Val Gly Asp Gly Cys Lys Ala Ala Leu Ser Leu Tyr Ser Asp
                    310
                                        315
                                                             320
Thr Ile Ser Ser Lys Lys
                325
```

<210> 281

<211> 309

<212> PRT

<213> Ureaplasma parvum

Met Asn Gln Glu Val Tyr Asp Leu Val Ile Ile Gly Ala Gly Pro Ala Gly Leu Ala Ala Val Tyr Ala Lys Arg Ser Gly Leu Asn Val Ile Ile Val Glu Lys Gln Phe Pro Gly Gly Lys Ile Ala Leu Thr Ser Asn Val Glu Asn Tyr Leu Gly Ile Asn Ser Ile Pro Gly Pro Glu Leu Ala . 60 Tyr Lys Met Tyr Glu Gln Val Leu Asn Leu Asn Val Ser Ile Ile Tyr Glu Ala Ala Asp Glu Ile Ser Leu Lys Glu Lys Tyr Lys Lys Ile Lys Leu Thr Thr Gln Thr Leu Ile Thr Lys Thr Val Ile Ile Ala Thr Gly Thr Glu Asn Arg Arg Leu Asn Ile Leu Gly Glu Leu Glu Phe Glu Asn Lys Gly Ile Ser Tyr Cys Ala Ile Cys Asp Gly Pro Leu Tyr Lys Asn Lys Ala Val Ser Val Ile Gly Ser Gly Asn Ser Ala Val Glu Glu Ala Ile Tyr Leu Ala Thr Ile Ala Lys Glu Val His Leu Ile Ala Asn Lys Pro Gln Phe Lys Ala Glu Gln Gln Leu Val Gln Ile Ala Asn Asn Thr Pro Asn Ile Lys Ile Tyr Tyr Asn Lys Gln Thr Phe Glu Phe Phe Gly His Gln Phe Leu Glu Gly Leu Lys Phe Arg Asp Leu Ile Thr Asn Glu Val Thr Thr Leu Asn Ile Glu Ala Asn Phe Thr Phe Ile Gly Leu Leu Pro Ser Arg Ile Asn Thr Asn Asn Leu Cys Ile Phe Asn Glu Val Asn Gly Phe Ile Thr Thr Asp Lys Asn Met Gln Thr Ser Val Cys Gly Ile Phe Ala Ala Gly Asp Ile Val Asp Lys Asn Val Arg Gln Ile Ala Thr

```
280
Ala Thr Asn Asp Gly Val Ile Ala Ala Leu Tyr Ala Lys Glu Tyr Ile
                        295
Thr Arg Asn Asn Trp
305
<210> 282
<211> 318
<212> PRT
<213> Vibrio cholerae
<400> 282
Met Ser Asn Val Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro
                                    10
Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Lys Pro
            20
Val Leu Val Thr Gly Met Gln Gln Gly Gln Leu Thr Thr Thr Thr
                            40
Glu Val Glu Asn Trp Pro Gly Asp Ala Glu Gly Leu Thr Gly Pro Ala
                        55
Leu Met Glu Arg Met Lys Glu His Ala Glu Arg Phe Asp Thr Glu Ile
Val Phe Asp His Ile Asn Ser Val Asp Leu Ser Ser Arg Pro Phe. Arg
               85
                                    90
Leu Thr Gly Asp Ser Gln Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ser
            100
                                105
Thr Gly Ala Ser Ala Lys Tyr Leu Gly Leu Glu Ser Glu Glu Ala Phe
                            120
Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr
                        135
                                           140 ·
Arg Asn Gln Lys Val Ala Val Val Gly Gly Gly Asn Thr Ala Val Glu
                   150
                                        155
Glu Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Val His
                165
                                    170
Arg Arg Asp Ser Phe Arg Ser Glu Lys Ile Leu Ile Asp Arg Leu Met
                                185
Asp Lys Val Ala Asn Gly Asn Ile Val Leu His Thr His Arg Thr Leu
        195
                            200
                                                205
Asp Glu Val Leu Gly Asp Glu Met Gly Val Thr Gly Val Arg Leu Lys
                        215
                                            220
Asp Thr Gln Ser Asp Met Thr Glu Asn Leu Asp Val Met Gly Val Phe
                    230
                                        235
Ile Ala Ile Gly His Gln Pro Asn Ser Gln Ile Phe Glu Gly Gln Leu
                245
                                    250
Glu Met Lys Asn Gly Tyr Ile Val Val Lys Ser Gly Leu Glu Gly Asn
           260
                                265
Ala Thr Gln Thr Ser Ile Glu Gly Val Phe Ala Ala Gly Asp Val Met
       275
                            280
                                                285
Asp His Asn Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys Met
                        295
                                            300
Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Ser Gln Gly Lys
<210> 283
<211> 321
<212> PRT
<213> Xylella fastidiosa
<400> 283
Met Ser Asp Tyr Pro Ala Ser Ala Lys His Ser Arg Leu Leu Ile Leu
                                    10
Gly Ser Gly Pro Ala Gly Trp Thr Ala Ala Val Tyr Ala Ala Arg Ala
Asn Leu Gln Pro Val Leu Ile Thr Gly Leu Gln Gln Gly Gln Leu
```

Met Thr Thr Glu Val Asp Asn Trp Pro Gly Asp Ala His Gly Leu Met Gly Pro Asp Leu Met Glu Arg Met Gln Ala His Ala Glu Arg Phe 70 Asp Thr Lys Val Ile Phe Asp Gln Ile Tyr Lys Ala Asp Leu Ser Thr 90 85 Arg Pro Phe Thr Leu Phe Gly Asp Ser Gly Leu Tyr Thr Cys Asp Gly 100 105 110 Leu Ile Ile Ala Thr Gly Ala Asn Ala Lys Tyr Leu Gly Ile Pro Ser 120 125 Glu Glu Ala Phe Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp 135 140 Gly Phe Phe Tyr Arg Asp Gln Asp Val Ala Val Ile Gly Gly Asn 150 155 Thr Ala Val Glu Glu Ala Leu Tyr Leu Ser Asn Ile Ala Arg Lys Val 170 165 Tyr Leu Ile His Arg Arg Asp Lys Leu Arg Ala Glu Lys Ile Met Gln 185 180 Asn Lys Leu Phe Ser Lys Ala Ala Thr Gly Lys Ile Glu Leu Ile Trp 195 200 205 Asn Asn Ala Val Glu Glu Val Leu Gly Asn Asp Ala Ser Val Thr' Gly 215 220 Val Arg Ile Arg Ser Thr Gln Asp Ser Ser Thr Arg Asp Ile Asp Val 230 235 Gln Gly Leu Phe Val Ala Ile Gly His His Pro Asn Thr Asp Leu Phe 250 245 Ala Gly Gln Leu Ala Met Asn Asn Gly Tyr Leu Gln Ile His Ser Gly 260 265 Thr Ala Gly Asn Val Thr Gln Thr Ser Val Glu Gly Val Phe Ala Ala 275 280 Gly Asp Val Ala Asp Gln His Tyr Arg Gln Ala Ile Thr Ser Ala Gly 295 300 Phe Gly Cys Met Ala Ala Leu Asp Ala Glu Arg Phe Leu Asp Lys Gly 315 Asn

<210> 284 <211> 318 <212> PRT

<213> Zymomonas mobilis

<400> 284 Met Ser Ala Asp Pro Ile Ser Thr Arg Val Phe Ile Leu Gly Ser Gly Pro Ala Gly Leu Thr Ala Ala Ile Tyr Ala Ala Arg Ala Gly Leu Asn 25 20 Pro Ile Val Ala Gln Gly Leu Gln Pro Gly Gly Gln Leu Thr Ile Thr 40 45 Thr Glu Val Glu Asn Phe Pro Gly Phe Arg Glu Pro Ile Gln Gly Pro 55 Trp Leu Met Glu Glu Met Gln Ala Gln Ala Glu Asn Val Gly Ala Lys 75 Leu Val Trp Asp Ile Ile Thr Ser Val Asp Phe Ser Gln Arg Pro Tyr 85 90 Arg Leu Met Gly Asp Gly Gly Gln Val Tyr Leu Ala Asp Ser Leu Ile 100 105 Ile Ser Thr Gly Ala Gln Ala Arg Trp Leu Gly Leu Glu Ser Glu Thr 120 Ala Leu Arg Gly Lys Gly Ile Ser Ala Cys Ala Thr Cys Asp Gly Phe 135 140 Phe Phe Arg Gly Lys Lys Val Val Ile Gly Gly Gly Asn Thr Ala 150 155 Val Glu Glu Ala Leu Tyr Leu Thr Asn His Ser Pro Glu Val Thr Leu 165 170 Ile His Arg Arg Asp Ser Leu Arg Ala Glu Lys Ile Met Gln Lys Arg

185 180 Leu Leu Ala Asn Pro Lys Ile Lys Ile Arg Trp Asn Ser Glu Val Ala 200 205 Glu Phe Ile Ala Gly Glu Asp Ser Ala Leu Ser Ala Val Lys Leu Lys 215 Asp Thr Lys Thr Gly Glu Glu Ser Leu Leu Glu Thr Glu Gly Ala Phe 230 235 Ile Ala Ile Gly His Lys Pro Ala Thr Glu Leu Phe Gln Gly His Leu 250 Lys Leu Asp Asp Glu Gly Tyr Ile Glu Val Thr Pro Gly Thr Thr Gln 265 Thr Ser Ile Lys Gly Ile Phe Ala Cys Gly Asp Val Met Asp Lys His 280 285 275 Tyr Arg Gln Ala Val Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu 295 300 Glu Ala Glu Arg Phe Leu Gly Glu Ile Asp Phe Lys Glu Asp

<210> 285 <211> 122 <212> PRT

<213> Bos taurus

<400> 285 Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Thr Asp Ser 5 Arg Lys Phe Gly Trp Glu Tyr Ser Gln Gln Val Arg His Ser Trp Ala 25 Thr Met Thr Glu Ala Ile Gln Ser His Ile Gly Ser Leu Ser Trp Gly 40 His Arg Leu Ala Leu Arg Glu Lys Ala Val Thr Tyr Val Asn Ser Phe 60 55 Gly Glu Phe Val Glu His His Lys Val Lys Ala Thr Asn Glu Lys Gly 70 75 Gln Glu Val Leu Tyr Thr Ala Ala Lys Phe Val Ile Ala Thr Gly Glu 90 85 Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Arg Glu Tyr Cys Ile Thr 100 105 Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys

<210> 286 <211> 511 <212> PRT <213> Bos taurus

<213> BOS Caurus

<400> 286 Met Ala Ala Leu Arg Gly Ala Ala Ala Arg Phe Arg Gly Arg Ala Pro Gly Gly Ala Arg Gly Ala Ala Gly Arg Gln Cys Tyr Asp Leu Leu Val Ile Gly Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln 40 Leu Gly Lys Lys Val Ala Val Leu Asp Tyr Val Glu Pro Ser Pro Gln 55 60 Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gly Met Ile Arg 85 90 Asp Ala Pro His Tyr Gly Trp Gly Val Ala Gln Ala Pro His Ser Trp 105 Ala Thr Leu Ala Asp Ala Val Gln Asn His Val Lys Ser Leu Asn Trp 120 125 Gly His Arg Ile Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Val

```
Lys Ala Ser Phe Val Asp Thr His Thr Val Cys Gly Val Ser Lys Gly
                    150
                                        155
Gly Glu Glu Thr Leu Leu Ser Ala Glu His Ile Val Ile Ala Thr Gly
                165
                                    170
Gly Arg Pro Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly
                               185
Ile Thr Ser Asp Asp Leu Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr
       195
                            200
                                                205
Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Leu Leu
                        215
                                            220
Thr Gly Leu Gly Leu Asp Thr Thr Val Met Ile Arg Ser Val Pro Leu
                    230
                                        235
Arg Ala Phe Asp Gln Gln Met Ala Ser Leu Val Thr Glu His Met Ala
                245
                                    250
Gly His Gly Thr Arg Ile Leu Arg Gly Cys Ala Pro Glu Lys Val Glu
            260
                                265
Lys Leu Pro Gly Gln Gln Leu Arg Val Thr Trp Val Asp Leu Thr Ser
                           280
Asp Arg Lys Asp Ala Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly
                        295
Arg Val Pro Glu Thr Ala Ser Leu Asn Leu Glu Lys Ala Gly Val His
                    310
                                        315
Thr Asn Pro Val Thr Gly Lys Ile Leu Val Asp Ala Gln Glu Thr Thr
               325
                                    330
Ser Val Pro His Ile Tyr Ala Ile Gly Asp Val Ala Glu Gly Arg Pro
           340
                                345
                                                    350
Glu Leu Thr Pro Thr Ala Ile Met Ala Gly Arg Leu Leu Ala Gln Arg
       355
                                                365
                           360
Leu Ser Gly Arg Thr Ser Asp Leu Met Asp Tyr Ser Ser Val Pro Thr
                        375
                                           380
Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu
                    390
                                        395
Ala Ala Val Ala Arg His Gly Glu Glu His Val Glu Val Tyr His Ala
               405
                                    410
Phe Tyr Lys Pro Leu Glu Phe Thr Val Pro Gln Arg Asp Ala Ser Gln
           420
                               425
Cys Tyr Ile Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu
       435
                            440
Gly Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Ile Gln Gly Phe
                       455
                                           460
Ala Leu Gly Ile Lys Cys Gly Ala Ser Tyr Gln Gln Leu Met Arg Thr
                   470
                                       475
Val Gly Ile His Pro Thr Cys Ala Glu Glu Val Ala Lys Leu Arg Ile
               485
                                   490
Ser Lys Arg Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Cys Gly
```

<210> 287

<211> 525

<212> PRT

<213> Caenorhabditis elegans

<220>

<221> VARIANT

<222> 524

<223> Xaa = Any Amino Acid

<400> 287

```
Ser Pro Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val
                    70
Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu Gly His
                85
                                    90
Ser Ile His Asp Ala Lys Lys Tyr Gly Trp Lys Leu Pro Glu Gly Lys
            100
                                105
Val Glu His Gln Trp Asn His Leu Arg Asp Ser Val Gln Asp His Ile
                            120
                                                125
Ala Ser Leu Asn Trp Gly Tyr Arg Val Gln Leu Arg Glu Lys Thr Val
                        135
                                            140
Thr Tyr Ile Asn Ser Tyr Gly Glu Phe Thr Gly Pro Phe Glu Ile Ser
                    150
                                        155
Ala Thr Asn Lys Lys Lys Val Glu Lys Leu Thr Ala Asp Arg Phe
                165
                                    170
Leu Ile Ser Thr Gly Leu Arg Pro Lys Tyr Pro Glu Ile Pro Gly Val
            180
                                185
Lys Glu Tyr Thr Ile Thr Ser Asp Leu Phe Gln Leu Pro Tyr Ser
                            200
Pro Gly Lys Thr Leu Cys Val Gly Ala Ser Tyr Val Ser Leu Glu Cys
                       215
                                           220
Ala Gly Phe Leu His Gly Phe Gly Phe Asp Val Thr Val Met Val Arg
                    230
                                        235
Ser Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Glu Arg Ile Arg
                245
                                    250
Lys His Met Ile Ala Tyr Gly Met Lys Phe Glu Ala Gly Val Pro Thr
            260
                                265
                                                    270
Arg Ile Glu Gln Ile Asp Glu Lys Thr Asp Glu Lys Ala Gly Lys Tyr
        275
                           280
                                                285
Arg Val Phe Trp Pro Lys Lys Asn Glu Glu Thr Gly Glu Met Gln Glu
                        295
                                            300
Val Ser Glu Glu Tyr Asn Thr Ile Leu Met Ala Ile Gly Arg Glu Ala
                    310
                                        315
Val Thr Asp Asp Val Gly Leu Thr Thr Ile Gly Val Glu Arg Ala Lys
                325
                                    330
Ser Lys Lys Val Leu Gly Arg Arg Glu Gln Ser Thr Thr Ile Pro Trp
            340
                                345
Val Tyr Ala Ile Gly Asp Val Leu Glu Gly Thr Pro Glu Leu Thr Pro
                            360
Val Ala Ile Gln Ala Gly Arg Val Leu Met Arg Arg Ile Phe Asp Gly
                        375
                                           380
Ala Asn Glu Leu Thr Glu Tyr Asp Gln Ile Pro Thr Thr Val Phe Thr
                   390
                                       395
Pro Leu Glu Tyr Gly Cys Cys Gly Leu Ser Glu Glu Asp Ala Met Met
                405
                                    410
Lys Tyr Gly Lys Asp Asn Ile Ile Ile Tyr His Asn Val Phe Asn Pro
                                425
Leu Glu Tyr Thr Ile Ser Glu Arg Met Asp Lys Asp His Cys Tyr Leu
                           440
        435
                                                445
Lys Met Ile Cys Leu Arg Asn Glu Glu Glu Lys Val Val Gly Phe His
                       455
                                            460
Ile Leu Thr Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Gly Ile Ala
                   470
                                        475
Leu Lys Leu Ala Ala Lys Lys Ala Asp Phe Asp Arg Leu Ile Gly Ile
                                    490
His Pro Thr Val Ala Glu Asn Phe Thr Thr Leu Thr Leu Glu Lys Lys
                               505
Glu Gly Asp Glu Glu Leu Gln Ala Ser Gly Cys Xaa Gly
                            520
```

<sup>&</sup>lt;210> 288

<sup>&</sup>lt;211> 667

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Caenorhabditis elegans

<sup>&</sup>lt;220>

<sup>&</sup>lt;221> VARIANT

<222> 666 <223> Xaa = Any Amino Acid

<400> 288 Met Lys Ser Leu Thr Glu Leu Phe Gly Cys Phe Lys Arg Gln Pro Arg Gln Glu Ala Ser Ser Pro Ala Asn Pro His Val Ser Asp Thr Leu Ser Met Gly Val Ala Ala Ser Gly Met Pro Pro Pro Lys Arg Pro Ala Pro Ala Glu Ser Pro Thr Leu Pro Gly Glu Thr Leu Val Asp Ala Pro Gly Ile Pro Leu Lys Glu Ala Leu Lys Glu Ala Ala Asn Ser Lys Ile Val Ile Phe Tyr Asn Ser Ser Asp Glu Glu Lys Gln Leu Val Glu Phe Glu Thr Tyr Leu Asn Ser Leu Lys Glu Pro Ala Asp Ala Glu Lys Pro Leu Glu Ile Pro Glu Ile Lys Lys Leu Gln Val Ser Arg Ala Ser Gln Lys Val Ile Gln Tyr Leu Thr Leu His Thr Ser Trp Pro Leu Met Tyr Ile Lys Gly Asn Ala Val Gly Gly Leu Lys Glu Leu Lys Ala Leu Lys Gln Asp Tyr Leu Lys Glu Trp Leu Arg Asp His Thr Tyr Asp Leu Ile Val Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ser Arg Leu Gly Lys Lys Val Ala Cys Leu Asp Phe Val Lys Pro Ser Pro Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu Gly His Ser Ile His Asp Ala Lys Lys Tyr Gly Trp Lys Leu Pro Glu Gly Lys Val Glu His Gln Trp Asn His Leu Arg Asp Ser Val Gln Asp His Ile Ala Ser Leu Asn Trp Gly Tyr Arg Val Gln Leu Arg Glu Lys Thr Val Thr Tyr Ile Asn Ser Tyr Gly Glu Phe Thr Gly Pro Phe Glu Ile Ser Ala Thr Asn Lys Lys Lys Val Glu Lys Leu Thr Ala Asp Arg Phe Leu Ile Ser Thr Gly Leu Arg Pro Lys Tyr Pro Glu Ile Pro Gly Val Lys Glu Tyr Thr Ile Thr Ser Asp Asp Leu Phe Gln Leu Pro Tyr Ser Pro Gly . Lys Thr Leu Cys Val Gly Ala Ser Tyr Val Ser Leu Glu Cys Ala Gly Phe Leu His Gly Phe Gly Phe Asp Val Thr Val Met Val Arg Ser Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Glu Arg Ile Arg Lys His Met Ile Ala Tyr Gly Met Lys Phe Glu Ala Gly Val Pro Thr Arg Ile Glu Gln Ile Asp Glu Lys Thr Asp Glu Lys Ala Gly Lys Tyr Arg Val Phe Trp Pro Lys Lys Asn Glu Glu Thr Gly Glu Met Gln Glu Val Ser Glu Glu Tyr Asn Thr Ile Leu Met Ala Ile Gly Arg Glu Ala Val Thr Asp Asp Val Gly Leu Thr Thr Ile Gly Val Glu Arg Ala Lys Ser Lys Lys Val Leu Gly Arg Arg Glu Gln Ser Thr Thr Ile Pro Trp Val Tyr Ala Ile Gly Asp Val Leu Glu Gly Thr Pro Glu Leu Thr Pro Val Ala

```
500
                                505
Ile Gln Ala Gly Arg Val Leu Met Arg Arg Ile Phe Asp Gly Ala Asn
                            520
Glu Leu Thr Glu Tyr Asp Gln Ile Pro Thr Thr Val Phe Thr Pro Leu
                       535
                                           540
Glu Tyr Gly Cys Cys Gly Leu Ser Glu Glu Asp Ala Met Met Lys Tyr
                   550
                                      555
Gly Lys Asp Asn Ile Ile Ile Tyr His Asn Val Phe Asn Pro Leu Glu
                                   570
               565
Tyr Thr Ile Ser Glu Arg Met Asp Lys Asp His Cys Tyr Leu Lys Met
                               585
Ile Cys Leu Arg Asn Glu Glu Glu Lys Val Val Gly Phe His Ile Leu
                           600
                                               605
Thr Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Gly Ile Ala Leu Lys
                       615
                                           620
Leu Ala Ala Lys Lys Ala Asp Phe Asp Arg Leu Ile Gly Ile His Pro
                                      635
                  630
Thr Val Ala Glu Asn Phe Thr Thr Leu Thr Leu Glu Lys Lys Glu Gly
              645
                                   650
Asp Glu Glu Leu Gln Ala Ser Gly Cys Xaa Gly
           660
```

<210> 289

<211> 516

<212> PRT

<213> Drosophila melanogaster

<400> 289 Met Ser Thr Ile Lys Phe Leu Arg Ser Ser Thr His Asn Ala Leu Arg 10 Ser Ser Leu Gly Trp Cys Arg Leu Ala Ala Ser Arg Pro Arg Tyr Asp 25 Tyr Asp Leu Val Val Leu Gly Gly Gly Ser Ala Gly Leu Ala Cys Ala Lys Glu Ala Ala Gly Cys Gly Ala Arg Val Leu Cys Phe Asp Tyr Val 55 Lys Pro Thr Pro Val Gly Thr Lys Trp Gly Ile Gly Gly Thr Cys Val 70 75 Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu 85 90 Gly Glu Ala Val His Glu Ala Val Ala Tyr Gly Trp Asn Val Asp Asp 105 Thr Asn Ile Arg Pro Asp Trp Arg Lys Leu Val Arg Ser Val Gln Asn 120 125 His Ile Lys Ser Val Asn Trp Val Thr Arg Val Asp Leu Arg Asp Lys 135 140 Lys Val Glu Tyr Val Asn Ser Met Ala Thr Phe Arg Asp Ser His Thr 150 155 Ile Glu Tyr Val Ala Met Pro Gly Ala Glu His Arg Gln Val Thr Ser 170 Glu Tyr Val Val Val Ala Val Gly Gly Arg Pro Arg Tyr Pro Asp Ile 185 190 Pro Gly Ala Val Glu Leu Gly Ile Thr Ser Asp Asp Ile Phe Ser Tyr 200 205 Glu Arg Glu Pro Gly Arg Thr Leu Val Val Gly Ala Gly Tyr Val Gly 215 220 Leu Glu Cys Ala Cys Phe Leu Lys Gly Leu Gly Tyr Glu Pro Thr Val 230 235 Met Val Arg Ser Ile Val Leu Arg Gly Phe Asp Arg Gln Met Ser Glu 250 245 255 Leu Leu Ala Ala Met Met Thr Glu Arg Gly Ile Pro Phe Leu Gly Thr 265 270 Thr Ile Pro Lys Ala Val Glu Arg Gln Ala Asp Gly Arg Leu Leu Val 280 Arg Tyr Arg Asn Thr Thr Gln Met Asp Gly Ser Asp Val Phe Asp

```
Thr Val Leu Trp Ala Ile Gly Arg Lys Gly Leu Ile Glu Asp Leu Asn
                    310
                                        315
Leu Asp Ala Ala Gly Val Lys Thr His Asp Asp Lys Ile Val Val Asp
                325
                                    330
Ala Ala Glu Ala Thr Ser Val Pro His Ile Phe Ala Val Gly Asp Ile
            340
                               .345
Ile Tyr Gly Arg Pro Glu Leu Thr Pro Val Ala Ile Leu Ser Gly Arg
        355
                           360
                                                365
Leu Leu Ala Arg Arg Leu Phe Ala Gly Ser Thr Gln Leu Met Asp Tyr
                        375
                                            380
Ala Asp Val Ala Thr Thr Val Phe Thr Pro Leu Glu Tyr Ser Cys Val
                    390
                                        395
Gly Met Ser Glu Glu Thr Ala Ile Glu Leu Arg Gly Ala Asp Asn Ile
                405
                                    410
                                                        415
Glu Val Phe His Gly Tyr Tyr Lys Pro Thr Glu Phe Phe Ile Pro Gln
                                425
Lys Ser Val Arg His Cys Tyr Leu Lys Ala Val Ala Glu Val Ser Gly
                          440
       435
Asp Gln Lys Ile Leu Gly Leu His Tyr Ile Gly Pro Val Ala Gly Glu
                       455
                                           460
Val Ile Gln Gly Phe Ala Ala Ala Leu Lys Thr Gly Leu Thr Val Lys
                    470
                                        475
Thr Leu Leu Asn Thr Val Gly Ile His Pro Thr Thr Ala Glu Glu Phe
               485
                                   490
Thr Arg Leu Ser Ile Thr Lys Arg Ser Gly Arg Asp Pro Thr Pro Ala
           500
                                505
Ser Cys Cys Ser
       515
<210> 290
<211> 524
<212> PRT
<213> Homo sapiens
<220>
<221> VARIANT
<222> 523
<223> Xaa = Any Amino Acid
Met Ala Ala Met Ala Val Ala Leu Arg Gly Leu Gly Gly Arg Phe Arg
                                    10
Trp Arg Thr Gln Ala Val Ala Gly Gly Val Arg Gly Ala Ala Arg Gly
           20
                                25
Ala Ala Ala Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly Gly
                            40
Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys
                        55
Val Ser Val Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr Arg Trp
                    70
Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu
                                    90
Met His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn
                                105
Tyr Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg'Lys Met
                                                125
       115
                           120
Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg
                       135
   130
                                           140
Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser
                    150
                                        155
Phe Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu
```

170

190

205

Ile Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro

185 Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser 200

165

```
Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val
                        215
Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile
                  230
                                        235
Gly Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe
               245
                                   250
                                                        255
Asp Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly
                                265
Thr Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg Leu Pro
        275
                                               285
                           280
Asp Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu
                        295
                                            300
Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro
                    310
Asp Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro
                325
                                   330
Asp Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro
                                                 350
            340
                                345
His Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr
        355
                            360
Pro Ile Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly
                        375
                                            380
Gly Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe
                    390
                                       395
Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val
                405
                                    410
Ala Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys
           420
                               425
Pro Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val
       435
                           440
                                                445
Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His
                        455
                                            460
Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly
                   470
                                        475
Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile
                                                        495
               485
                                    490
His Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg
          500
                               505
Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Xaa Gly
```

<210> 291

<211> 497

<212> PRT

<213> Homo sapiens

<400> 291

Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala 25 Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 35 40 45 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 55 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His 85 90 Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 105 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 120 Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn 135 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala

```
150
                                       155
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
               165
                                   170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
            180
                            185
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                       200
Leu Ala Gly Ile Gly Leu Asn Val Thr Val Met Val Arg Ser Ile Leu
                     215
                                           220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                   230
                                       235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val
                                   250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln
           260
                               265
                                                  270
Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met
       275
                           280
                                               285
Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr
                      295
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                 310
                                       315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                                   330
               325
                                                       335
Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
                               345
Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu
                           360
       355
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly
                      375
                                           380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                  390
                                      395
Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg
               405
                                   410
Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn
           420
                               425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                           440
                                              445
Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln
                       455
                                           460
Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr
                  470
                                      475
Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Arg Ile Leu Gln Ala Gly
           485
```

<210> 292 <211> 497 <212> PRT

<213> Homo sapien

<400> 292

Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Pro Ala Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Gly Thr Pro Thr Pro 35 40 45 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 55 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His 85 90 Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 100 105 110

```
Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu
                            120
Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn
                                           140
                       135
Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala
                   150
                                       155
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
                                   170
               165
                                                       175
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
                               185
            180
                                                   190
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                           200
                                               205
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
                        215
                                           220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                   230
                                     235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val
               245
                                  250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln
                               265
                                                   270
Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met
                           280
                                               285
Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr
                        295
                                           300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                                       315
                   310
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                                  330
              325
                                                       335
Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
           340
                               345
                                                   350
Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu
                           360
                                               365
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly
                       375
                                           380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                                       395
                   390
Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg
               405
                                   410
                                                       415
Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn
          420
                               425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                           440
Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln
                       455
                                          460
Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr
                   470
                         · 475
Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly
```

```
<210> 293

<211> 521

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 520

<223> Xaa = Any Amino Acid

<400> 293
```

Met Ala Val Ala Leu Arg Gly Leu Gly Gly Arg Phe Arg Trp Arg Thr 1 5 10 15
Gln Ala Val Ala Gly Gly Val Arg Gly Ala Ala Arg Gly Ala Ala Ala 20 25 30

Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys Val Ala Val Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn Tyr Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg Lys Met Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser Phe Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu Ile Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile Gly Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe Asp Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly Thr Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg Leu Pro Asp Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro Asp Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro Asp Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro His Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr Pro Ile Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly Gly Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val Ala Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys Pro Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile His Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Xaa Gly

<sup>&</sup>lt;210> 294 <211> 579

<sup>&</sup>lt;212> PRT

<213> Homo sapiens <220> <221> VARIANT <222> 578 <223> Xaa = Any Amino Acid <400> 294 Ala Glu Arg Val Val Ile Phe Ser Lys Ser Tyr Cys Pro His Ser Thr 10 Arg Val Lys Glu Leu Phe Ser Ser Leu Gly Val Glu Cys Asn Val Leu 20 25 Glu Leu Asp Gln Val Asp Asp Gly Ala Arg Val Gln Glu Val Leu Ser 40 35 Glu Ile Thr Asn Gln Lys Thr Val Pro Asn Ile Phe Val Asn Lys Val 55 His Val Gly Gly Cys Asp Gln Thr Phe Gln Ala Tyr Gln Ser Gly Leu 70 75 Leu Gln Lys Leu Leu Gln Glu Asp Leu Ala Tyr Asp Tyr Asp Leu Ile 90 Ile Ile Gly Gly Ser Gly Gly Leu Ser Cys Ala Lys Glu Ala Ala 100 105 Ile Leu Gly Lys Lys Val Met Val Leu Asp Phe Val Val Pro Ser Pro 115 120 Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 135 140 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 150 155 Cys Asp Ser Arg Lys Phe Gly Trp Glu Tyr Asn Gln Gln Val Arg His 165 170 Asn Trp Glu Thr Met Thr Lys Ala Ile Gln Asn His Ile Ser Ser Leu 185 180 190 Asn Trp Gly Tyr Arg Leu Ser Leu Arg Glu Lys Ala Val Ala Tyr Val 195 200 205 200 205 Asn Ser Tyr Gly Glu Phe Val Glu His His Lys Ile Lys Ala Thr Asn 215 220 Lys Lys Gly Gln Glu Thr Tyr Tyr Thr Ala Ala Gln Phe Val Ile Ala 230 235 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Gln Gly Asp Lys Glu Tyr 250 245 Cys Ile Thr Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 260 265 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 280 285 Leu Ala Gly Phe Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 295 300 Leu Arg Gly Phe Asp Gln Glu Met Ala Glu Lys Val Gly Ser Tyr Met 310 315 Glu Gln His Gly Val Lys Phe Leu Arg Lys Phe Ile Pro Val Met Val 325 330 Gln Gln Leu Glu Lys Gly Ser Pro Gly Lys Leu Lys Val Leu Ala Lys 340 345 Ser Thr Glu Gly Thr Glu Thr Ile Glu Gly Val Tyr Asn Thr Val Leu 355 360 365 Leu Ala Ile Gly Arg Asp Ser Cys Thr Arg Lys Ile Gly Leu Glu Lys 375 380 Ile Gly Val Lys Ile Asn Glu Lys Ser Gly Lys Ile Pro Val Asn Asp 390 395 Val Glu Gln Thr Asn Val Pro Tyr Val Tyr Ala Val Gly Asp Ile Leu 405 410 Glu Asp Lys Pro Glu Leu Thr Pro Val Ala Ile Gln Ser Gly Lys Leu 420 . 425 430 Leu Ala Gln Arg Leu Phe Gly Ala Ser Leu Glu Lys Cys Asp Tyr Ile 440 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly Leu Ser Glu Glu Lys Ala Ile Glu Val Tyr Lys Lys Glu Asn Leu Glu

```
465
                    470
                                        475
Ile Tyr His Thr Leu Phe Trp Pro Leu Glu Trp Thr Val Ala Gly Arg
                485
                                    490
                                                       495
Glu Asn Asn Thr Cys Tyr Ala Lys Ile Ile Cys Asn Lys Phe Asp His
                               505
           500
Asp Arg Val Ile Gly Phe His Ile Leu Gly Pro Asn Ala Gly Glu Val
        515
                            520
Thr Gln Gly Phe Ala Ala Ala Met Lys Cys Gly Leu Thr Lys Gln Leu
                        535
Leu Asp Asp Thr Ile Gly Ile His Pro Thr Cys Gly Glu Val Phe Thr
                   550
                                      555
Thr Leu Glu Ile Thr Lys Ser Ser Gly Leu Asp Ile Thr Gln Lys Gly
Cys Xaa Gly
```

<210> 295 <211> 524 <212> PRT <213> Homo sapien <220> <221> VARIANT <222> 523

<223> Xaa = Any Amino Acid

<400> 295 Met Ala Ala Met Ala Val Ala Leu Arg Gly Leu Gly Gly Arg Phe Arg 10 Trp Arg Thr Gln Ala Val Ala Gly Gly Val Arg Gly Ala Ala Arg Gly 20 25 Ala Ala Ala Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly Gly 40 Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys 55 60 Val Ala Val Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr Arg Trp 70 Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu 90 Met His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn 105 Tyr Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg Lys Met 120 115 125 Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg 135 140 Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser 150 155 Phe Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu 170 165 Ile Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro 180 185 190 Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser 195 200 205 Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val 215 220 Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile 235 230 Gly Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe 245 250 Asp Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly 265 270 Thr Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg Leu Pro 280 285 Asp Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu 295

Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro

```
305
                                       315
                    310
Asp Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro
                                  330
               325
                                                       335
Asp Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro
           340
                               345
                                                   350
His Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr
       355
                           360
Pro Ile Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly
                       375
                                           380
Gly Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe
                                     395
                   390
Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val
                405
                                   410
Ala Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys
           420
                               425
Pro Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val
                           440
       435
                                               445
Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His
                       455
                                           460
Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly
                                       475
                   470
Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile
                                   490
               485
                                                       495
His Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg
           500
                               505
Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Xaa Gly
                           520
```

<210> 296

<211> 577

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> 576

<223> Xaa = Any Amino Acid

<400> 296

Arg Val Val Ile Phe Ser Lys Ser Tyr Cys Pro His Ser Thr Arg Val 10 15 Lys Glu Leu Phe 'Ser Ser Leu Gly Val Glu Cys Asn Val Leu Glu Leu Asp Gln Val Asp Asp Gly Ala Arg Val Gln Glu Val Leu Ser Glu Ile 40 Thr Asn Gln Lys Thr Val Pro Asn Ile Phe Val Asn Lys Val His Val 55 60 Gly Gly Cys Asp Gln Thr Phe Gln Ala Tyr Gln Ser Gly Leu Leu Gln 75 70 Lys Leu Leu Gln Glu Asp Leu Ala Tyr Asp Tyr Asp Leu Ile Ile 85 90 Gly Gly Gly Ser Gly Gly Leu Ser Cys Ala Lys Glu Ala Ala Ile Leu 105 Gly Lys Lys Val Met Val Leu Asp Phe Val Val Pro Ser Pro Gln Gly 125 115 120 Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro 135 140 Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Cys Asp 150 155 Ser Arg Lys Phe Gly Trp Glu Tyr Asn Gln Gln Val Arg His Asn Trp 165 170 Glu Thr Met Thr Lys Ala Ile Gln Asn His Ile Ser Ser Leu Asn Trp 190 180 185 Gly Tyr Arg Leu Ser Leu Arg Glu Lys Ala Val Ala Tyr Val Asn Ser 205 195 200 Tyr Gly Glu Phe Val Glu His His Lys Ile Lys Ala Thr Asn Lys Lys

```
210
                        215
                                           220
Gly Gln Glu Thr Tyr Tyr Thr Ala Ala Gln Phe Val Ile Ala Thr Gly
                230
                                      235
Glu Arg Pro Arg Tyr Leu Gly Ile Gln Gly Asp Lys Glu Tyr Cys Ile
               245
                                    250
Thr Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys Pro Leu
                               265
Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Ala
       275
                           280
                                               285
Gly Phe Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu Leu Arg
                       295
                                           300
Gly Phe Asp Gln Glu Met Ala Glu Lys Val Gly Ser Tyr Met Glu Gln
                   310
                                       315
His Gly Val Lys Phe Leu Arg Lys Phe Ile Pro Val Met Val Gln Gln
              325
                                   330
                                                       335
Leu Glu Lys Gly Ser Pro Gly Lys Leu Lys Val Leu Ala Lys Ser Thr
           340
                               345
                                                   350
Glu Gly Thr Glu Thr Ile Glu Gly Val Tyr Asn Thr Val Leu Leu Ala
                            360
Ile Gly Arg Asp Ser Cys Thr Arg Lys Ile Gly Leu Glu Lys Ile Gly
                       375
                                           380
Val Lys Ile Asn Glu Lys Ser Gly Lys Ile Pro Val Asn Asp Val Glu
                   390
                                       395
Gln Thr Asn Val Pro Tyr Val Tyr Ala Val Gly Asp Ile Leu Glu Asp
                405
                                   410
                                                       415
Lys Pro Glu Leu Thr Pro Val Ala Ile Gln Ser Gly Lys Leu Leu Ala
    . 420
                              425
                                                   430
Gln Arg Leu Phe Gly Ala Ser Leu Glu Lys Cys Asp Tyr Ile Asn Val
                                              445
       435
                           440
Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly Leu Ser
                        455
                                           460
Glu Glu Lys Ala Ile Glu Val Tyr Lys Lys Glu Asn Leu Glu Ile Tyr
                   470
                                       475
His Thr Leu Phe Trp Pro Leu Glu Trp Thr Val Ala Gly Arg Glu Asn
               485
                                   490
                                                       495
Asn Thr Cys Tyr Ala Lys Ile Ile Cys Asn Lys Phe Asp His Asp Arg
           500
                               505
                                                   510
Val Ile Gly Phe His Ile Leu Gly Pro Asn Ala Gly Glu Val Thr Gln
       515
                           520
                                              525
Gly Phe Ala Ala Ala Met Lys Cys Gly Leu Thr Lys Gln Leu Leu Asp
                                           540
                       535
Asp Thr Ile Gly Ile His Pro Thr Cys Gly Glu Val Phe Thr Thr Leu
                   550
                                       555
Glu Ile Thr Lys Ser Ser Gly Leu Asp Ile Thr Gln Lys Gly Cys Xaa
            - 565
                                   570
Gly
```

<210> 297 <211> 494

<213> Homo sapien

<400> 297

<212> PRT

Met Glu Asp Gln Ala Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly 10 Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly 20 Arg Lys Val Ala Val Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr 40 Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala 75 Pro Asn Tyr Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg 90

```
Lys Met Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly
                                105
His Arg Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys
                           120
        115
                                                125
Ala Ser Phe Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly
                       135
Lys Glu Ile Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly
                    150
                                        155
Arg Pro Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile
               165
                                    170
                                                        175
Thr Ser Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu
            180
                               185
Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr
                            200
                                              205
Gly Ile Gly Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg
                    215
                                           220
Gly Phe Asp Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser
                   230
                                       235
His Gly Thr Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg
                                                       255
                245
                                   250
Leu Pro Asp Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly
           260
                                265
                                                   270
Lys Glu Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg
       275
                            280
Val Pro Asp Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr
                        295
                                           300
Ser Pro Asp Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser
                  310
                                       315
Val Pro His Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu
               325
                                   330
Leu Thr Pro Thr Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu
                                345
Phe Gly Gly Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr
       355
                           360
                                               365
Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu
                       375
                                           380
Ala Val Ala Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His
                   390
                                       395
Tyr Lys Pro Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys
               405
                                   410
Tyr Val Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly
                               425
           420
                                                   430
Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala
       435
                           440 .
                                               445
Leu Gly Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val
                       455
                                           460
Gly Ile His Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser
                  470
                                       475
Lys Arg Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Cys Gly
               485
```

<210> 298

<211> 521

<212> PRT

<213> Homo sapien

<400> 298

 Met Ala Ala Met Ala Val Ala Leu Arg Gly Leu Gly Gly Arg Phe Arg

 1
 5
 10
 15

 Trp Arg Thr Gln Ala Val Ala Gly Gly Val Arg Gly Ala Ala Arg Gly
 20
 25
 30

 Ala Ala Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly Gly Gly Ser
 45

 Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys Val
 50

 Ser Val Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr Arg Trp Gly

```
70
Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met
                                9.0
              85
His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn Tyr
                               105
Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg Lys Met Ala
                           120
                                              125
Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg Val
                       135
                                          140
Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser Phe
                   150
                                       155
Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu Ile
              165
                                  170
                                                       175
Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro Arg
           180
                               185
                                                   190
Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser Asp
                           200
Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val Gly
                      215
                                         220
Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile Gly
                   230
                                      235
Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe Asp
               245
                                   250
Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly Thr
                            265
Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Lys Arg Leu Pro Asp
                                              285
                     280
Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu Asp
                       295
Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro Asp
                   310
                                       315
Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro Asp
               325
                                  330
Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro His
          340
                               345
                                                   350
Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr Pro
                          360
Thr Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly Gly
                       375
                                           380
Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe Thr
                   390
                                      395
Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val Ala
               405
                                   410
Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys Pro
                              425
Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val Lys
                          440
                                              445
Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His Phe
                     455
                                          460
Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly Ile
                   470
                                       475
Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile His
                                  490
Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg Ser
          500
                              505
Gly Leu Asp Pro Thr Val Thr Gly Cys
       515
```

```
<210> 299
```

<sup>&</sup>lt;211> 549

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapien

<sup>&</sup>lt;400> 299

Met Ser Cys Glu Asp Gly Arg Ala Leu Glu Gly Thr Leu Ser Glu Leu

1 5 10 15

Ala Ala Glu Thr Asp Leu Pro Val Val Phe Val Lys Gln Arg Lys Ile Gly Gly His Gly Pro Thr Leu Lys Ala Tyr Gln Glu Gly Arg Leu Gln Lys Leu Leu Lys Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly Cys

545

<210> 300 <211> 613 <212> PRT <213> Mus musculus <220> <221> VARIANT <222> 612 <223> Xaa = Any Amino Acid <400> 300 Met Pro Val Asp Asp Cys Trp Leu Tyr Phe Pro Ala Ser Arg Gly Arg 10 15 Thr Phe Val Gln Thr Val Trp Val Ala Pro Thr Cys Pro Asn Cys Cys 25 Trp Phe Pro Gly Phe Leu Pro Pro Val Pro Arg Pro Pro His Val Pro 40 Arg Val Leu Leu Arg Gly Pro Arg Gly Ala Val Leu Pro Ala Ser Arg 55 60 Pro Ser Lys Thr Leu Pro Ser Ser Ser Gln Thr Pro Cys Pro Thr Asp 70 75 Pro Cys Ile Cys Pro Pro Pro Ser Thr Pro Asp Ser Arg Gln Glu Lys 85 90 Asn Thr Gln Ser Glu Leu Pro Asn Lys Lys Gly Gln Leu Gln Lys Leu 105 Pro Thr Met Asn Gly Ser Lys Asp Pro Pro Gly Ser Tyr Asp Phe Asp 125 120 Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu 135 140 Ala Ala Lys Phe Asp Lys Lys Val Leu Val Leu Asp Phe Val Thr Pro 150 155 Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val 170 165 175 Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln 180 185 Ala Leu Lys Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Asp Thr Val 200 Lys His Asp Trp Glu Lys Met Thr Glu Ser Val Gln Ser His Ile Gly 215 220 Ser Leu Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val 230 235 Tyr Glu Asn Ala Tyr Gly Arg Phe Ile Gly Pro His Arg Ile Val Ala 245 250 255 Thr Asn Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu 265 Ile Ala Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys 275 280 Glu Tyr Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro 295 300 Gly Lys Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala 310 315 Gly Phe Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser 330 325 , 335 Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu 345 340 His Met Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr 360 365 Lys Ile Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Thr 375 380 Ala Gln Ser Thr Asn Ser Glu Glu Thr Ile Glu Gly Glu Phe Asn Thr 390 395 Val Leu Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu 410 405 415 Glu Thr Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val

420 425 Thr Asp Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp 440 Ile Leu Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly 455 Arg Leu Leu Ala Gln Arg Leu Tyr Gly Gly Ser Asn Val Lys Cys Asp 470 475 Tyr Asp Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys 490 485 Cys Gly Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn 505 500 510 Ile Glu Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro 520 Ser Arg Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Leu Lys 535 540 Asp Asp Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly 550 555 Glu Val Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys 565 570 Gln Gln Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile 585 580 Phe Thr Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln 595 600 Ser Gly Cys Xaa Gly

<210> 301

<211> 310

<212> PRT

<213> Mus musculus

<400> 301 Met Asn Gly Ser Lys Asp Pro Pro Gly Ser Tyr Asp Phe Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Lys Glu Ala Ala 25 Lys Phe Asp Lys Lys Val Leu Val Leu Asp Phe Val Thr Pro Thr Pro 35 40 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 75 Lys Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Asp Thr Val Lys His 90 Asp Trp Glu Lys Met Thr Glu Ser Val Gln Ser His Ile Gly Ser Leu 105 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 120 125 Asn Ala Tyr Gly Arg Phe Ile Gly Pro His Arg Ile Val Ala Thr Asn 135 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala 150 155 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 170 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro, Gly Lys 180 185 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 200 205 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 215 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 235 230 Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile 245 250 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Thr Ala Gln 260 265

Ser Thr Asn Ser Glu Glu Thr Ile Glu Gly Glu Phe Asn Thr Val Leu
275
280
285

Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr
290
295
300

Val Gly Val Lys Ile Asn
305
310

<210> 302 <211> 613 <212> PRT <213> Mus musculus

VZZJ/ Mas mascare

<400> 302 Met Ser Ser Pro Pro Gly Arg Arg Ala Arg Leu Ala Ser Pro Gly Thr Ser Arg Pro Ser Ser Glu Ala Arg Glu Glu Leu Arg Arg Arg Leu Arg 20 25 Asp Leu Ile Glu Gly Asn Arg Val Met Ile Phe Ser Lys Ser Tyr Cys 40 Pro His Ser Thr Arg Val Lys Glu Leu Phe Ser Ser Leu Gly Val Val 55 60 Tyr Asn Ile Leu Glu Leu Asp Gln Val Asp Asp Gly Ala Ser Val Gln 75 70 Glu Val Leu Thr Glu Ile Ser Asn Gln Lys Thr Val Pro Asn Ile Phe 85 90 Val Asn Lys Val His Val Gly Gly Cys Asp Arg Thr. Phe Gln Ala His 105 Gln Asn Gly Leu Leu Gln Lys Leu Leu Gln Asp Asp Ser Ala His Asp 125 115 120 Tyr Asp Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ser Cys Ala 135 140 Lys Glu Ala Ala Asn Leu Gly Lys Lys Val Met Val Leu Asp Phe Val 150 Val Pro Ser Pro Gln Gly Thr Thr Trp Gly Leu Gly Gly Thr Cys Val 170 175 165 Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu 180 185 Gly His Ala Leu Gln Asp Ala Lys Lys Tyr Gly Trp Glu Tyr Asn Gln 200 205 Gln Val Lys His Asn Trp Glu Ala Met Thr Glu Ala Ile Gln Ser His 215 Ile Gly Ser Leu Asn Trp Gly Tyr Arg Val Thr Leu Arg Glu Lys Gly 230 235 Val Thr Tyr Val Asn Ser Phe Gly Glu Phe Val Asp Leu His Lys Ile 250 245 Lys Ala Thr Asn Lys Lys Gly Gln Glu Thr Phe Tyr Thr Ala Ser Lys 265 Phe Val Ile Ala Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Gln Gly 275 280 Asp Lys Glu Tyr Cys Ile Thr Ser Asp Asp Leu Phe Ser Leu Pro Tyr 295 300 Cys Pro Gly Cys Thr Leu Val Val Gly Ala Ser Tyr Val Gly Leu Glu 310 315 Cys Ala Gly Phe Leu Ala Gly Leu Gly Leu Asp Val Thr Val Met Val 330 Arg Ser Val Leu Leu Arg Gly Phe Asp Gln Glu Met Ala Glu Lys Val 345 Gly Ser Tyr Leu Glu Gln Gln Gly Val Lys Phe Gln Arg Lys Phe Thr 355 365 360 Pro Ile Leu Val Gln Gln Leu Glu Lys Gly Leu Pro Gly Lys Leu Lys 375 380 Val Val Ala Lys Ser Thr Glu Gly Pro Glu Thr Val Glu Gly Ile Tyr 390 395 Asn Thr Val Leu Leu Ala Ile Gly Arg Asp Ser Cys Thr Arg Lys Ile 405 410 Gly Leu Glu Lys Ile Gly Val Lys Ile Asn Glu Lys Asn Gly Lys Ile

```
420
                               425
Pro Val Asn Asp Val Glu Gln Thr Asn Val Pro His Val Tyr Ala Ile
                        440
Gly Asp Ile Leu Asp Gly Lys Pro Glu Leu Thr Pro Val Ala Ile Gln
                      455
                                        460
Ala Gly Lys Leu Leu Ala Arg Arg Leu Phe Gly Val Ser Leu Glu Lys
                   470
                                       475
Cys Asp Tyr Ile Asn Ile Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr
                                  490
Gly Cys Cys Gly Leu Ser Glu Glu Lys Ala Ile Glu Met Tyr Lys Lys
          500
                              505
                                                  510
Glu Asn Leu Glu Val Tyr His Thr Leu Phe Trp Pro Leu Glu Trp Thr
      515
                           520
                                              525
Val Ala Gly Arg Asp Asn Asn Thr Cys Tyr Ala Lys Ile Ile Cys Asn
                      535
Lys Phe Asp Asn Glu Arg Val Val Gly Phe His Leu Leu Gly Pro Asn .
                 550
                                    555
Ala Gly Glu Ile Thr Gln Gly Phe Ala Ala Ala Met Lys Cys Gly Leu
               565
                                   570
                                                      575
Thr Lys Gln Leu Leu Asp Asp Thr Ile Gly Ile His Pro Thr Cys Gly
                             585
Glu Val Phe Thr Thr Leu Glu Ile Thr Lys Ser Ser Gly Leu Asp Ile
      595
                          600
Thr Gln Lys Gly Cys
 610
```

<210> 303

<211> 524

<212> PRT

<213> Mus musculus

<220>

<221> VARIANT

<222> 523

<223> Xaa = Any Amino Acid

<400> 303

Met Val Ala Ala Met Val Ala Ala Leu Arg Gly Pro Ser Arg Arg Phe 10 Arg Pro Arg Thr Arg Ala Leu Thr Arg Gly Thr Arg Gly Ala Ala Ser 20 25 Ala Ala Gly Gly Gln Gln Ser Phe Asp Leu Leu Val Ile Gly Gly 40 Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Lys Lys 55 60 Val Ala Val Ala Asp Tyr Val Glu Pro Ser Pro Arg Gly Thr Lys Trp 70 75 Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu 85 90 Met His Gln Ala Ala Leu Leu Gly Gly Met Ile Arg Asp Ala His His 105 Tyr Gly Trp Glu Val Ala Gln Pro Val Gln His Asn Trp Lys Thr Met 120 125 Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg 135 140 Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser 150 155 Phe Val Asp Glu His Thr Val Arg Gly Val Asp Lys Gly Gly Lys Ala 165 170 Thr Leu Leu Ser Ala Glu His Ile Val Ile Ala Thr Gly Gly Arg Pro 180 185 190 Arg Tyr Pro Thr Gln Val Lys Gly Ala Leu Glu Tyr Gly Ile Thr Ser 195 200 Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val 215 220 Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile

```
225
                    230
                                        235
Gly Leu Asp Thr Thr Val Met Met Arg Ser Ile Pro Leu Arg Gly Phe
               245
                                  250
Asp Gln Gln Met Ser Ser Leu Val Thr Glu His Met Glu Ser His Gly
                               265
Thr Gln Phe Leu Lys Gly Cys Val Pro Ser His Ile Lys Lys Leu Pro
                           280
                                               285
Thr Asn Gln Leu Gln Val Thr Trp Glu Asp His Ala Ser Gly Lys Glu
                       295
                                           300
Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro
                   310
                                       315
Glu Thr Arg Thr Leu Asn Leu Glu Lys Ala Gly Ile Ser Thr Asn Pro
             325
                                  330
Lys Asn Gln Lys Ile Ile Val Asp Ala Gln Glu Ala Thr Ser Val Pro
           340
                               345
His Ile Tyr Ala Ile Gly Asp Val Ala Glu Gly Arg Pro Glu Leu Thr
                           360
                                               365
Pro Thr Ala Ile Lys Ala Gly Lys Leu Leu Ala Gln Arg Leu Phe Gly
                       375
                                           380
Lys Ser Ser Thr Leu Met Asp Tyr Ser Asn Val Pro Thr Thr Val Phe
                   390
                                       395
Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val
               405
                                   410
Ala Leu His Gly Gln Glu His Val Glu Val Tyr His Ala Tyr Tyr Lys
          420
                                                   430
                             425
Pro Leu Glu Phe Thr Val Ala Asp Arg Asp Ala Ser Gln Cys Tyr Ile
                           440
       435
Lys Met Val Cys Met Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His
                       455
Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly
                  470
                                       475
Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Gln Thr Val Gly Ile
               485
                                   490
                                                       495
His Pro Thr Cys Ser Glu Glu Val Val Lys Leu His Ile Ser Lys Arg
           500
                               505
Ser Gly Leu Glu Pro Thr Val Thr Gly Cys Xaa Gly
```

<210> 304

<211> 528

<212> PRT

<213> Mus musculus

<220>

<221> VARIANT

<222> 527

<223> Xaa = Any Amino Acid

<400> 304

Met Ala Ala Met Val Ala Gly Arg Met Trp Ala Ala Leu Arg Gly Pro 10 Ser Arg Arg Phe Arg Pro Arg Thr Arg Ala Leu Thr Arg Gly Thr Arg 20 25 Gly Ala Ala Ser Ala Ala Gly Gly Gln Gln Ser Phe Asp Leu Leu Val 40 Ile Gly Gly Ger Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln 55 60 Leu Gly Lys Lys Val Ala Val Ala Asp Tyr Val Glu Pro Ser Pro Arg 70 75 Gly Thr Lys Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile 85 90 Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gly Met Ile Arg 105 Asp Ala His His Tyr Gly Trp Glu Val Ala Gln Pro Val Gln His Asn 115 120 125 Trp Lys Thr Met Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn

```
130
                        135
                                            140
Trp Gly His Arg Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn
                150
                                       155
Ile Lys Ala Ser Phe Val Asp Glu His Thr Val Arg Gly Val Asp Lys
                                    170
Gly Gly Lys Ala Thr Leu Leu Ser Ala Glu His Ile Val Ile Ala Thr
                                185
Gly Gly Arg Pro Arg Tyr Pro Thr Gln Val Lys Gly Ala Leu Glu Tyr
        195
                            200
                                                205
Gly Ile Thr Ser Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys
                        215
                                           220
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                   230
                                        235
Leu Thr Gly Ile Gly Leu Asp Thr Thr Val Met Met Arg Ser Ile Pro
               245
                                   250
                                                       255
Leu Arg Gly Phe Asp Gln Gln Met Ser Ser Leu Val Thr Glu His Met
                                265
Glu Ser His Gly Thr Gln Phe Leu Lys Gly Cys Val Pro Ser His Ile
                            280
Lys Lys Leu Pro Thr Asn Gln Leu Gln Val Thr Trp Glu Asp His Ala
                                           300
                       295
Ser Gly Lys Glu Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile
                   310
                                       315 .
Gly Arg Val Pro Glu Thr Arg Thr Leu Asn Leu Glu Lys Ala Gly Ile
                325
                                    330
Ser Thr Asn Pro Lys Asn Gln Lys Ile Ile Val Asp Ala Gln Glu Ala
           340
                               345
Thr Ser Val Pro His Ile Tyr Ala Ile Gly Asp Val Ala Glu Gly Arg
                           360
       355
                                               365
Pro Glu Leu Thr Pro Thr Ala Ile Lys Ala Gly Lys Leu Leu Ala Gln
                        375
                                            380
Arg Leu Phe Gly Lys Ser Ser Thr Leu Met Asp Tyr Ser Asn Val Pro
                   390
                                       395
Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu
                                   410
               405
Glu Glu Ala Val Ala Leu His Gly Gln Glu His Val Glu Val Tyr His
           420
                                425
                                                   430
Ala Tyr Tyr Lys Pro Leu Glu Phe Thr Val Ala Asp Arg Asp Ala Ser
       435
                           440
Gln Cys Tyr Ile Lys Met Val Cys Met Arg Glu Pro Pro Gln Leu Val
                       455
                                           460
Leu Gly Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly
                   470
                                       475
Phe Ala Leu Gly Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Gln
              . 485
                                   490
Thr Val Gly Ile His Pro Thr Cys Ser Glu Glu Val Val Lys Leu His
                               505
Ile Ser Lys Arg Ser Gly Leu Glu Pro Thr Val Thr Gly Cys Xaa Gly
```

<210> 305 <211> 520

<212> PRT <213> Mus musculus

```
Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala
Ala Leu Leu Gly Gly Met Ile Arg Asp Ala His His Tyr Gly Trp Glu
            100
                                105
                                                    110
Val Ala Gln Pro Val Gln His Asn Trp Lys Thr Met Ala Glu Ala Val
                            120
                                                 125
Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg Val Gln Leu Gln
                        135
Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser Phe Val Asp Glu
                    150
                                        155
His Thr Val Arg Gly Val Asp Lys Gly Gly Lys Ala Thr Leu Leu Ser
                165
                                    170
Ala Glu His Ile Val Ile Ala Thr Gly Gly Arg Pro Arg Tyr Pro Thr
                                185
Gln Val Lys Gly Ala Leu Glu Tyr Gly Ile Thr Ser Asp Asp Ile Phe
        195
                            200
                                                205
Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val Gly Ala Ser Tyr
                        215
                                            220
Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile Gly Leu Asp Thr
                    230
                                       235
Thr Val Met Met Arg Ser Ile Pro Leu Arg Gly Phe Asp Gln Gln Met
                245
                                    250
                                                        255
Ser Ser Leu Val Thr Glu His Met Glu Ser His Gly Thr Gln Phe Leu
            260
                                265
                                                    270
Lys Gly Cys Val Pro Ser His Ile Lys Lys Leu Pro Thr Asn Gln Leu
                           280
        275
                                                285
Gln Val Thr Trp Glu Asp His Ala Ser Gly Lys Glu Asp Thr Gly Thr
                        295
Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro Glu Thr Arg Thr
                    310
                                        315
Leu Asn Leu Glu Lys Ala Gly Ile Ser Thr Asn Pro Lys Asn Gln Lys
                325
                                    330
                                                        335
Ile Ile Val Asp Ala Gln Glu Ala Thr Ser Val Pro His Ile Tyr Ala
            340
                                345
Ile Gly Asp Val Ala Glu Gly Arg Pro Glu Leu Thr Pro Thr Ala Ile
                            360
Lys Ala Gly Lys Leu Leu Ala Gln Arg Leu Phe Gly Lys Ser Ser Thr
                        375
                                            380
Leu Met Asp Tyr Ser Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu
                    390
                                        395
Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val Ala Leu His Gly
                405
                                    410
Gln Glu His Val Glu Val Tyr His Ala Tyr Tyr Lys Pro Leu Glu Phe
            420
                                425
                                                    430
Thr Val Ala Asp Arg Asp Ala Ser Gln Cys Tyr Ile Lys Met Val Cys
       435
                           440
                                               445
Met Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His Phe Leu Gly Pro
                       455
                                            460
Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly Ile Lys Cys Gly
                    470
                                        475
Ala Ser Tyr Ala Gln Val Met Gln Thr Val Gly Ile His Pro Thr Cys
                                    490
Ser Glu Glu Val Val Lys Leu His Ile Ser Lys Arg Ser Gly Leu Glu
           500
                               505
Pro Thr Val Thr Gly Cys Cys Gly
       515
                            520
```

<210> 306 <211> 499 <212> PRT

<213> Mus musculus

```
25
Lys Phe Asp Lys Lys Val Leu Val Leu Asp Phe Val Thr Pro Thr Pro
                           40
Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys
Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu
Lys Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Asp Thr Val Lys His
                85
                                   90
Asp Trp Glu Lys Met Thr Glu Ser Val Gln Ser His Ile Gly Ser Leu
            100
                               105
Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu
                           120
                                               125
Asn Ala Tyr Gly Arg Phe Ile Gly Pro His Arg Ile Val Ala Thr Asn
                     135
                                           140
Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala
                   150
                                       155
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
                                    170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
           180
                               185
                                                   190
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
 195
                           200
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
                       215
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                   230
                                       235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile
                                   250
               245
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Thr Ala Gln
           260
                               265
Ser Thr Asn Ser Glu Glu Thr Ile Glu Gly Glu Phe Asn Thr Val Leu
                           280
       275
Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr
                       295
                                           300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                  310
                                      315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
               325
                                   330
Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
                               345
Leu Ala Gln Arg Leu Tyr Gly Gly Ser Asn Val Lys Cys Asp Tyr Asp
                          360
                                               365
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly
                       375
                                           380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                   390
                                      395
Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg
                                 410
Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Leu Lys Asp Asp
           420
                               425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                           440
Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Gln Gln
                       455
                                           460
Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr
                  470
                                     475
Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly
Cys Cys Gly
```

<sup>&</sup>lt;210> 307

<sup>&</sup>lt;211> 497

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Rattus norvegicus

<220> <221> VARIANT <222> 497 <223> Xaa = Any Amino Acid Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr Asp Phe Asp Leu Ile .10 Ile Ile Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala Lys Phe Asp Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro Leu Gly Thr Asn Gly Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 55 60 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu Asp Thr Val Lys His 90 Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn His Ile Gly Ser Leu 105 100 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 115 120 Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys Ile Met Ala Thr Asn 135 140 Asn Lys Gly Lys Glu Lys Val Tyr Ser Ala Glu Arg Phe Leu Ile Ala 155 150 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 165 170 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 185 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 200 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 215 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 230 235 Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile 250 245 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Lys Val Thr Ala Lys 265 270 Ser Thr Asn Ser Glu Glu Thr Ile Glu Asp Glu Phe Asn Thr Val Leu 275 280 285 Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr 295 300 Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp 310 315 Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu 325 330 Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu 340 345 350 Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Asp 360 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly 375 380 Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu 395 390 Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg 405 410 Asp Asn Asn Lys Cys Tyr Ala Lys Val Ile Cys Asn Leu Lys Asp Asn 420 425 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val 440 Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Gln Gln 455 460 Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr 470 475 Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly

485 490 495

Xaa

```
<210> 308
<211> 176
<212> PRT
<213> Rattus norvegicus
```

<400> 308 Arg Ile His Ala Gly Gly Ala Gly Arg Arg Arg Gly Gly Ala Arg Arg 1.0 Ala Gly Val Phe Ile Leu Leu Ala His Pro Asn Lys Lys Gly Leu Leu Arg Lys Leu Ser Thr Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr 40 Asp Phe Asp Leu Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala 55 60 Ala Lys Glu Ala Ala Lys Phe Asp Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys 90 85 Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu 100 105 Leu Gly Gln Ala Leu Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu 115 120 125 Asp Thr Val Lys His Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn 135 140 His Ile Gly Ser Leu Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys 150 155

Lys Val Val Tyr Glu Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys

170

<210> 309 <211> 498 <212> PRT <213> Rattus norvegicus

<220> <221> VARIANT <222> 497

<223> Xaa = Any Amino Acid

<400> 309 Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr Asp Phe Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Lys Glu Ala Ala Lys Phe Asp Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 35 40 Leu Gly Thr Asn Gly Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 75 Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu Asp Thr Val Lys His 85 90 Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn His Ile Gly Ser Leu 105 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 115 120 125 Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys Ile Met Ala Thr Asn 135 140 Asn Lys Gly Lys Glu Lys Val Tyr Ser Ala Glu Arg Phe Leu Ile Ala 155 150 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr

```
165
                                    170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
            180
                                185
                                                   190
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                            200
                                                205
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
                        215
                                            220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                    230
                                       235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile
                245
                                    250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Lys Val Thr Ala Lys
           260
                                265
                                                    270
Ser Thr Asn Ser Glu Glu Thr Ile Glu Asp Glu Phe Asn Thr Val Leu
                            280
                                                285
Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr
                        295
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                   310
                                        315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
               325
                                    330
                                                        335
Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
          340
                                345
Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Asp
                            360
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly
                        375
                                            380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                    390
                                        395
Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg
               405
                                    410
Asp Asn Asn Lys Cys Tyr Ala Lys Val Ile Cys Asn Leu Lys Asp Asn
            420
                                425
                                                    430
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                           440
                                               445
Thr Gln Ala Leu Gln Pro Leu Lys Cys Gly Leu Thr Lys Gln Gln Leu
                       455
                                           460
Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr Thr
                    470
                                        475
Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly Cys
                                    490
Xaa Gly
```

```
<210> 310
<211> 11
<212> PRT
```

<213> Rattus norvegicus

<400> 310 Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr 1 5 10

<210> 311 <211> 496 <212> PRT <213> Rattus norvegícus

```
Leu Gly Thr Asn Gly Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys
Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu
                                        75
                    70
Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu Asp Thr Val Lys His
                85
                                    90
Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn His Ile Gly Ser Leu
            100
                               105
Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu
                           120
                                               125
Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys Ile Met Ala Thr Asn
                      135
                                           140
Asn Lys Gly Lys Glu Lys Val Tyr Ser Ala Glu Arg Phe Leu Ile Ala
              150
                                       155
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
                165
                                    170
                                                       175
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
                               185
                                                   190
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                           200
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
                        215
                                            220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                   230
                                      235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile
               245
                                    250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Lys Val Thr Ala Lys
                               265
Ser Thr Asn Ser Glu Glu Thr Ile Glu Asp Glu Phe Asn Thr Val Leu
                           280
                                               285
Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr
                      295
                                           300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                   310
                                        315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                                  330
Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
                               345
Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Asp
                                               365
                           360
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly
                       375
                                           380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                   390
                                       395
Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg
              405
                                   410
Asp Asn Asn Lys Cys Tyr Ala Lys Val Ile Cys Asn Leu Lys Asp Asn
                               425
           420
                                                   430
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
                           440
Thr Gln Ala Leu Gln Pro Leu Lys Cys Gly Leu Thr Lys Gln Gln Leu
                       455
                                           460
Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr Thr
                   470
                                       475
Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly Cys
               485
                                   490
```

<sup>&</sup>lt;210> 312

<sup>&</sup>lt;211> 526

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Rattus norvegicus

<sup>&</sup>lt;220>

<sup>&</sup>lt;221> VARIANT

<sup>&</sup>lt;222> 525

<sup>&</sup>lt;223> Xaa = Any Amino Acid

<400> 312 Met Ala Ala Ile Val Ala Ala Leu Arg Gly Ser Ser Gly Arg Phe Arg Pro Gln Thr Arg Val Leu Thr Arg Gly Thr Arg Gly Ala Ala Gly Ala 20 25 Ala Ser Ala Ala Gly Gly Gln Gln Asn Phe Asp Leu Leu Val Ile Gly Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys Val Ala Val Ala Asp Tyr Val Glu Pro Ser Pro Arg Gly Thr Lys Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys 90 Lys Leu Met His Gln Ala Ala Leu Leu Gly Gly Met Ile Arg Asp Ala 105 110 Gln His Tyr Gly Trp Glu Val Ala Gln Pro Val Gln His Asn Trp Lys 115 120 125 Ala Met Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Tro Gly 135 His Arg Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys 150 155 Ala Ser Phe Val Asn Glu His Thr Val His Gly Val Asp Lys Ala Gly 165 170 Lys Val Thr Gln Leu Ser Ala Lys His Ile Val Ile Ala Thr Gly Gly 185 Arg Pro Lys Tyr Pro Thr Gln Val Lys Gly Ala Leu Glu His Gly Ile 200 Thr Ser Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu 215 220 Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr 230 235 Gly Ile Gly Leu Asp Thr Thr Val Met Met Arg Ser Val Pro Leu Arg 250 Gly Phe Asp Gln Gln Met Ala Ser Leu Val Thr Glu His Met Glu Ser 265 His Gly Thr Arg Phe Leu Lys Gly Cys Val Pro Ser Leu Ile Arg Lys 280 Leu Pro Thr Asn Gln Leu Gln Val Thr Trp Glu Asp Leu Ala Ser Gly 295 Lys Glu Asp Val Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg 310 Val Pro Glu Thr Arg Asn Leu Asn Leu Glu Lys Ala Gly Val Asn Thr 325 330 Asn Pro Lys Asn Gln Lys Ile Ile Val Asp Ala Gln Glu Ala Thr Ser 340 345 Val Pro His Ile Tyr Ala Ile Gly Asp Val Ala Glu Gly Arg Pro Glu 360 Leu Thr Pro Thr Ala Ile Lys Ala Gly Lys Leu Leu Ala Gln Arg Leu 375 380 Phe Gly Lys Ser Ser Thr Leu Met Asn Tyr Ser Asn Val Pro Thr Thr 390 395 Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu 405 410 Ala Val Ala Leu His Gly Gln Glu His Ile Glu Val Tyr His Ala Tyr 425 Tyr Lys Pro Leu Glu Phe Thr Val Ala Asp Arg Asp Ala Ser Gln Cys 440 Tyr Ile Lys Met Val Cys Met Arg Glu Pro Pro Gln Leu Val Leu Gly 455 460 Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala 470 475 Leu Gly Ile Gln Cys Gly Ala Ser Tyr Ala Gln Val Met Gln Thr Val 485 490 Gly Ile His Pro Thr Cys Ser Glu Glu Val Val Lys Leu His Ile Ser 500 505 Lys Arg Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Xaa Gly 520

```
<210> 313
<211> 499
<212> PRT
<213> Sus Scrofa
<220>
<221> VARIANT
<222> 498
<223> Xaa = Any Amino Acid
<400> 313
Met Asn Gly Ala Glu Glu Leu Pro Glu Met Tyr Asp Tyr Asp Leu Ile
                                    10
Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala
                                25
Arg Phe Asn Lys Arg Val Met Val Leu Asp Phe Val Thr Pro Thr Pro
        35
                            40
                                                45
Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Ser Cys
                        55
Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu
Arg Asp Ser Arg Asn Tyr Gly Trp Asn Val Glu Glu Thr Ile Lys His
                                   90
               85
Asp Trp Glu Arg Met Thr Glu Ala Val Gln Asn His Ile Gly Ser Leu
            100
                                105
                                                    110
Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Thr Tyr Glu
                            120
Asn Ala Tyr Gly Gln Phe Val Gly Pro His Arg Ile Lys Ala Thr Asn
                                            140
                        135
Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Lys Phe Leu Ile Ala
                   150
                                        155
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
                                    170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
                                185
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                            200
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
                       215
                                           220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                    230
                                        235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val
               245
                                   250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln
                               265
                                                    270
Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met
                            280
                                                285
Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr
                       295
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                                        315
                   310
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                                   330
               325
                                                        335
Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
                                345
Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu
                            360
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly
                                            380
                       375
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                    390
                                        395
Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg
                405
                                   410
Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn
           420
                               425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
```

Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln 450

Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr 465

Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly Cys Xaa Gly

Xaa Gly

## INTERNATIONAL SEARCH REPORT

It ational Application No PCT/US 01/50240

|  |  |  |   | , · <del>-</del>     |  |  |  |  |  |
|--|--|--|---|----------------------|--|--|--|--|--|
| A. CLASSI<br>IPC 7   | FICATION OF SUBJECT MATTER<br>C12N15/79  |  |   |                      |  |  |  |  |  |
| According to International Patent Classification (IPC) or to both national classification and IPC  |  |  |   |                      |  |  |  |  |  |
| B. FIELDS SEARCHED   |  |  |   |                      |  |  |  |  |  |
| Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N   |  |  |   |                      |  |  |  |  |  |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched .  |  |  |   |                      |  |  |  |  |  |
| Electronic data base consulted during the international search (name of data base and, where practical, search terms used)  EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE  |  |  |   |                      |  |  |  |  |  |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT   |  |  |   |                      |  |  |  |  |  |
| Category •   | Citation of document, with indication, where appropriate, of the re  | levant passages                                    |   | Relevant to dalm No. |  |  |  |  |  |
| X  | WO 98 53698 A (BOOTHE JOSEPH ;DEC<br>M (CA); GOLL JANIS (CA); MOLONEY<br>3 December 1998 (1998-12-03)<br>page 13, line 27 -page 14, line 4<br>1-42; example 11       | 1–266  |   |                      |  |  |  |  |  |
| X  | US 5 948 682 A (MOLONEY, MAURICE 7 September 1999 (1999-09-07) column 18, line 46 - line 55  | M.)  |   | 1–266                |  |  |  |  |  |
|  |  |  | ·   |                      |  |  |  |  |  |
| Further documents are listed in the continuation of box C.  Patent family members are listed in annex.   |  |  |   |                      |  |  |  |  |  |
| • Special categories of cited documents:  T later document published after the International filing date   |  |  |   |                      |  |  |  |  |  |
| Considered to be of particular relevance investigation of the carrier document but published on or after the international filing date "X" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another claim or other special reason (as specified) "Y" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another can be called the carrier or the carrier of the car |  |  | or priority date and not in conflict with the application but clied to understand the principle or theory underlying the invention  "document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such document. |                      |  |  |  |  |  |
| other means  'P' document published prior to the international filing date but later than the priority date claimed  'B' document published prior to the international filing date but later than the priority date claimed  'S' document member of the same patent family   |  |  |   |                      |  |  |  |  |  |
|  | actual completion of the international search  | Date of malling of the international search report |   |                      |  |  |  |  |  |
| 8  | May 2002   | 21/05/20   | 002   | •                    |  |  |  |  |  |
| Name and n   | railing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040. Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Authorized officer  Sprinks                        | , M   |                      |  |  |  |  |  |

## INTERNATIONAL SEARCH REPORT

information on patent family members

h atlonal Application No PCT/US 01/50240

| Patent document<br>cited in search report |   | Publication<br>date |      | Patent family member(s) | Publication date |
|---|---|---------------------|------|-------------------------|------------------|
| WO 9853698                                | A | 03-12-1998          | AU   | 737896 B2               | 06-09-2001       |
|   |   |                     | AU   | 7517898 A               | 30-12-1998       |
|   |   |                     | BR   | 9809691 A               | 03-10-2000       |
|   |   |                     | WO   | 9853698 A1              | 03-12-1998       |
|   |   |                     | CN   | 1258198 T               | 28-06-2000       |
|   |   |                     | EP   | 0986309 A1              | 22-03-2000       |
|   |   |                     | JP - | 2002503268 T            | 29-01-2002       |
|   |   |                     | NO   | 995802 A                | 26-01-2000       |
|   |   |                     | US   | 6146645 A               | 14-11-2000       |
|   |   |                     | US   | 6183762 B1              | 06-02-2001       |
|   |   |                     | US   | 6210742 B1              | 03-04-2001       |
|   |   |                     | US   | 2002037303 A1 .         | 28-03-2002       |
|   |   |                     | ZA   | 9804459 A               | 13-04-1999       |
| US 5948682                                | A | 07-09-1999          | US   | 5650554 A               | 22-07-1997       |
|   |   |                     | US   | 6288304 B1              | 11-09-2001       |
|   |   | •                   | ΑU   | 709141 B2               | 19-08-1999       |
|   |   | •                   | ΑU   | 4295096 A               | 24-07-1996       |
|   |   | •                   | BR   | 9600006 A               | 21-01-1998       |
|   |   |                     | CA,  | 2208751 A1              | 11-07-1996       |
|   |   |                     | WO   | 9621029 A1              | 11-07-1996       |
|   |   |                     | EP   | 0871749 A1              | 21-10-1998       |
|   |   |                     | ZA   | 9510999 A               | 13-07-1996       |
|   |   |                     | WO   | 9321320 A1              | 28-10-1993       |
|   |   |                     | WO   | 9320216 A1              | 14-10-1993       |